Development of Dissolution Test for Dronedarone Hydrochloride Pharmaceutical Formulation

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Abstract **- Formulation quality control aspects are mainly deals with evaluation of dissolution and drug release profile of drugs from various dosage forms. In this study a RP-HPLC method was developed and validated for the dissolution study of Dronedarone Hydrochloride from tablet formulation. The validated method was applied for any other formulation due to its acceptability as per the ICH guidelines. The various validation parameters pass the acceptance criteria as per the ICH guidelines.**

Index Terms **- Stability, RP-HPLC, Dissolution, Evaluation, Formulation, Dronedarone Hydrochloride.**

1.INTRODUCTION

Analytical method developed by the scientist is basically deals with complete description of the analytical procedure sufficiently detailed to enable persons “skilled in the art” to replicate it. The write-up includes all important operational parameters and specific instructions such as preparation of reagents, performance of system suitability tests, description of blanks used, precautions, and explicit formulas for calculation of test results. [1-3] these all factors equally reflect formation of good analytical method. As such newer and newer drug or drug combinations enters in market, analysis of such drugs/combinations is much important regarding determination of particular pharmaceuticals by development of respective analytical method. Primarily pharmaceutical company develops a method for their respected formulation but is not disclosed at all, so as concern to academic research students in their research institute tries to develop the methods in order to make easier analysis than earlier reported or tries in order to use of different techniques [4-6] e.g. instrumental or non-instrumental. Genuine rationale implies the identification of need for the procedure and describes the capability of the specific procedure proposed and why it is preferred over other types of determinations. For revised procedures, a comparison should be provided of limitations of the current compendia procedure and advantages offered by the proposed procedure.

The planed research work concerns with development of analytical procedures by instrumental technique, sorely deals with use of spectrophotometric and chromatographic techniques i.e. absorbance spectroscopy by utilizing UV spectrophotometer and separation technique relevant with HPLC. Now a day the use of these two tools is very common for determination of pharmaceuticals. And it is a duty of a research scientist to utilize such techniques to develop analytical methods for drug or drugs formulated as a single or combined dosage form in order to simplify the way of analysis of respective drugs.[5-9]

Literature survey reveals that very few UV spectroscopy methods and liquid chromatographic analytical methods has been reported for determination of Dronedarone hydrochloride; as in bulk or pharmaceutical dosages form. [10-13] this research work especially recounts the use of spectrophotometric technique and chromatographic technique to estimate a drug from pharmaceutical dosage form.

2 EXPERIMENTAL

2.1 Materials:

The chemical was purchased from MERCK, FISCHER SCIENTIFIC (QUALIGENS), RANKEM (RFCL), and are of HPLC Grade. The drug sample

Dronedarone Hydrochloride was procured from Micro labs Mumbai.

Table no. 01: Optimized chromatographic conditions	
Column	Hyper chrome ODS C18 column (250 x 4.6 mm)
Detection wavelength	290.0 nm
Flow rate	1.0 mL/min
Temperature	25ºC (Ambient)
pH	2.3
Injection volume	20 µL
Mobile phase	Acetonitrile: Triethylamine Solution (70:30)

2.2 Preparation of standard solution:
Standard stock solution:
An accurately weighed quantity of DDH (~25 mg) was transferred in a 50 mL volumetric flask, dissolved in sufficient quantity of diluents to prepare a standard stock (500 µg/mL)
Preparation of standard solution:
The standard stock solution was appropriately diluted with diluent to get the final concentration of 50 µg/mL

2.3 Linearity [15]
Aliquots of standard stock solution were diluted in range 3.5 to 6.5 ml in 50ml volumetric flask with diluent and volume was made up to mark with diluent to obtain concentration ranging from 70.0 – 120.0 µg/mL of Dronedarone hydrochloride.
Preparation of sample solution
Weigh and finely powdered 10 tablets and transfer the quantity of powder containing equivalent to 25mg of DDH to 50.0 mL volumetric flask, sonicated for 15 min with sufficient quantity of diluent and volume was made up to mark with diluent. The content of the flask was filtered through 0.45 µm membrane filter paper. A 1.0 mL with portion of the filtered was further diluted to 10.0 mL with diluent. After equilibration of stationary phase, five sample solutions were injected separately and chromatograms were recorded. The content of DDH in each sample was calculated by comparing the peak area of sample with that standard using formula,

$$\% \text{ Label Claim} = \frac{Au}{As} \times \frac{Wstd}{100} \times \frac{100}{Wtab} \times \frac{Avg.\ wt}{L.C.} \times P$$

Where,
Au = Peak area of sample
As = Peak area of standard
Wstd = Weight (mg) of DDH in std. stock
Wtab = Weight (mg) of tablets powder Avg. wt = Average weight of tablets
P = Potency of standard
L.C. =Label claim of drug in mg

2.4 Recovery studies
It was carried out by standard addition method
Preparation of sample:
An accurately weighed quantity of tablet powder equivalent to 25 mg of DDH was transferred to 50.0 mL volumetric flask and to it reference standard pure drug added at three different level, sonicated for 15 min, with sufficient quantity of diluent and volume was made up to the mark. The content was filtered through 0.45 µm membrane filter paper. A 1.0 mL portion of the filtered was further diluted to 10.0 mL with diluent.

2.5Accuracy:
Accuracy of the proposed method was ascertained on the basis of recovery studies performed by standard addition method. Results are shown in Table no. 03

2.6 Precision:
Precision of any analytical method was expressed as SD and %RSD of series of measurements. Precision of estimation of DDH by proposed method was ascertained by replicate analysis of homogeneous samples of tablets.

2.7 Linearity and Range:
Linearity of DDH was performed using the standard solution in the range of 70.0 µg/mL to 130.0 µg/mL (i.e. 70% to 130% of standard concentration). The correlation coefficient was found to be 0.999 for DDH

2.8Ruggedness:
Different analyst
The sample was prepared and analyzed as per the proposed method. The ruggedness of the proposed method has been verified by analyzing as tablet sample used for method precision by two different analysts using same instrument. The ruggedness results were compared with method precision data. The overall mean, standard deviation (SD) and %RSD of the assay values are shown in Table No.04

2.9Intraday and Interday variation:

The sample was prepared and analyzed as per the proposed method. After equilibration of stationary phase, sample solutions were injected separately at 0 Hr, 3 Hr, 5 Hr and the chromatograms were recorded. Similarly, the same solutions were injected on 1st, 3rd, 7th and 10 th day. The chromatograms so recorded and results were calculated. The contents of DDH were calculated by comparing the peak area of sample with that of standard using formula given under marketed formulation. Results are recorded in Table No. 05 & 06

2.10 Robustness:

The robustness of the method was evaluated by injecting the sample at deliberately varied the chromatographic conditions viz. composition of organic phase in mobile phase, pH by Triehtylamine solution 0.2unit, varying composition and wavelength 5nm. The system suitability was evaluated and amounts of DDH were calculated from sample solution in each varied condition. Results are tabulated in Table no. 07

3. RESULT AND DISCUSSION

The RP-HPLC method was developed and validated for the dissolution studies of DDH All the validation parameters are in the limit as per the ICH guidelines hence the proposed method can be used for the dissolution studies of DDH from its tablet formulations.

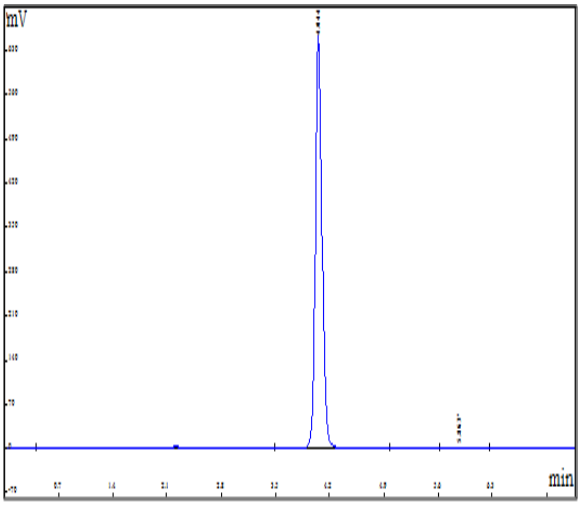
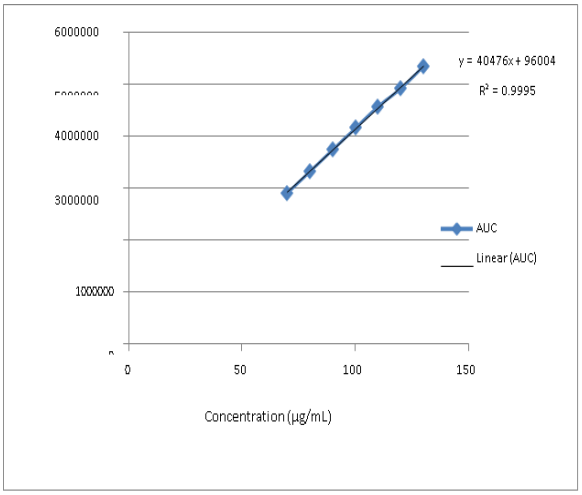


Fig.No.01: Standard chromatogram of Dronedarone hydrochloride



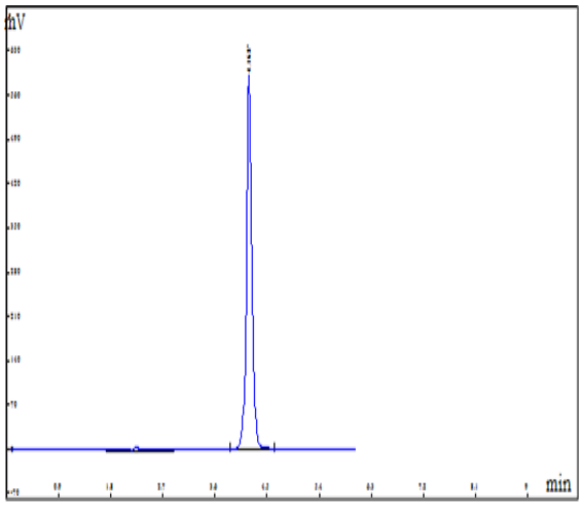


Fig.No.03: Chromatogram of formulation of Dronedarone hydrochloride

Table No.02: Estimation of DDH in formulation

Sr.No.	Wt. of std. taken (mg)	Wt. of tablet powder taken (mg)	Peak area of std. (mV)	Peak area of sample (mV)	% Label claim
1	25.0	42.8	4048308	4165814	99.46
S2		42.7		4142679	99.14
3		42.5		4174177	100.4
4		43.0		4194532	99.69
5		42.9		4201533	100.07
				Mean	100.14
				±S.D.	1.2
				%RSD	1.2

Table No. 03: Recovery study

Sr. No.	Amt. of pure drug added(mg)	Amt. recovered (mg)	% Recovery
1	20.0	19.69	98.47

2	25.0	24.87	99.48
3	30.0	29.46	98.20
		Mean	98.71
		±SD	0.67
		%RSD	0.68

Table No.04 : Ruggedness study (different analyst)

Sr.No.	% Estimation of DDH	
	Analyst-I	Analyst-II
1	98.30	101.09
2	100.79	99.65
3	99.64	100.32
Mean	99.57	100.35
±SD	1.24	0.72
%RSD	1.25	0.71

Table No.05: Intraday study

Time (Hr)	Wt. of tab. taken (mg)	A.U.C (mV)	% Label claim
0	42.8	4268634	100.81
3		4237452	100.08
5		4295841	98.98
		Mean	99.95
		±SD	0.92
		%RSD	0.92

Table No.06 : Interday study

Days	Wt. of tab. taken (mg)	A.U.C (mV)	% Label claim
Day 1	42.8	4268634	100.88
Day3		4237452	100.15
Day5		4147618	98.02
Day7		4162240	98.37
		Mean	99.35
		±SD	1.37
		%RSD	1.38

Table No.07: Robustness study

Sr. No.	Deliberate condition	Wt. tablet taken (mg)	Retention time (min)	Theoretical plate	Asymmetry
1	Standard condition	42.8	4.012	7565	1.23
2	Change in pH(2.1)		3.917	7360	1.38
3	Change in pH(2.5)		4.075	7415	1.34
4	Composition 77:23		3.689	7484	1.32
5	Composition 63:37		5.813	7801	1.40
6	Wavelength at 285nm		4.039	7546	1.36
7	Wavelength at 295nm		4.188	7423	1.35
				Mean	1.34
				SD	0.023
				%RSD	1.75

4. CONCLUSION

The results obtained by RP- HPLC method for determination of Dronedarone hydrochloride are reliable, accurate and precise. The method does not have any interference of excipients while determining from their formulation. Hence, can be employed for routine quality control analysis of Dronedarone hydrochloride in tablet form.

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