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Research Article

Difference Spectroscopic Method for the Estimation of Acebutolol Hydrochloride in Bulk and In its Formulation

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ABSTRACT

A simple, precise and accurate difference spectroscopic method has been developed for the estimation of Acebutolol Hydrochloride in bulk drug form by difference spectrophotometric method. Acebutolol Hydrochloride has exhibited maximum absorbance at about 233nm and 234nm in acidic and basic solution respectively. Beer's law was obeyed in the concentration range of 2-10 µg/ml in both the cases. The regression of coefficient was found to be r^2=0.9992. The LOD and LOQ value were found to be 0.2670ppm and 0.8091ppm respectively. The proposed method was successfully applied for the determination of Acebutolol Hydrochloride in bulk drug. As per ICH guidelines the result of the analysis were validated statistically and were found to be satisfactory.

Keywords: Acebutolol Hydrochloride, Validation, Hypertension, Spectrophotometer

INTRODUCTION

Chemically acebutolol hydrochloride is a (N-[3-Acetyl-4-[2-hydroxy-3[(1-methylethyl) amino] propoxy] phenyl] butanamide) hydrochloride is a cardio-selective betablocker used in the management of hypertension, angina pectoris and cardiac arrhythmias. Acebutolol hydrochloride (Fig.1.) is a cardioselective, hydrophilic β-adrenoreceptor blocking agent with mild intrinsic sympathomimetric activity (ISA) for use in treating patients with hypertension and ventricular arrhythmias[1].

Molecular Formula: $C_{18}H_{29}ClN_2O_4$.

Molecular weight: 372.9 g/mole

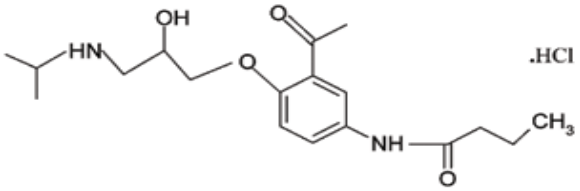

Figure 1. Structure of Acebutolol hydrochloride.

Objective:

Acebutolol hydrochloride shows improved absorbing interference by the technique of different spectrophotometry. Thus the objective of the present study was to develop new analytical difference spectrophotometry method and its validation parameters for the proposed method according to ICH guidelines for the estimation of Acebutolol hydrochloride bulk drug [2, 3, 4].

MATERIALS AND METHODS

Chemical and reagents:

Acebutolol hydrochloride [bulk drug] used were of analytical reagent grade purchased from research lab fine chem. industries Mumbai, India, NaOH and HCL were purchased from Poona chemical laboratory and double distilled water was used throughout the analysis.

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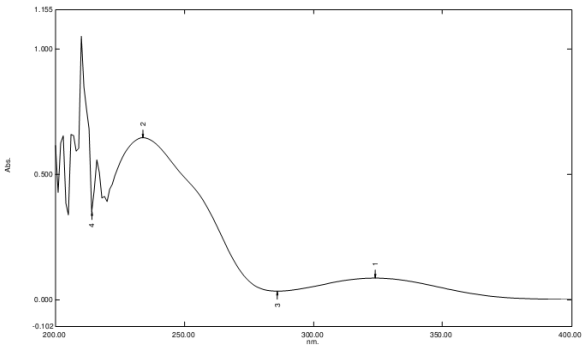
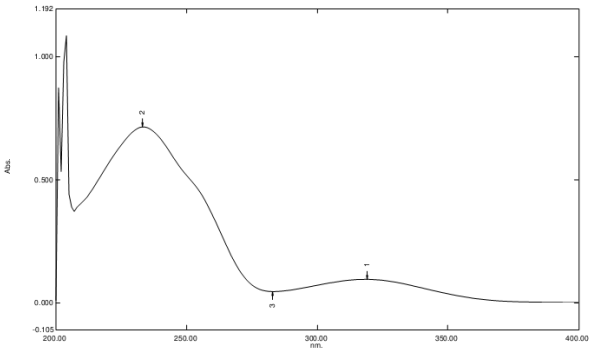
Instrumentation:
A shimadzu 1800 UV/VIS double beam spectrophotometer with 1cm matched quartz cells was used for all spectral measurements.

Selection of common solvents:
1N HCL and 1N NaOH were selected as a common solvent for developing spectral characteristics of drug.

Preparation of solution:
Standard stock solution containing Acebutolol hydrochloride was prepared by dissolving 10mg in 100ml of methanol and then diluted with 1N NaOH and 1N HCL separately to get series of dilution ranging from 2-10 µg/ml and then absorbance recorded at 233 nm and 234 nm respectively against reagent blank. Calibration curve was prepared by plotting concentration versus difference in absorbance and found to be linear in the concentration range of 2-10 µg/ml[2,3,4].



1N NaOH with λMax 233nm



1N HCL with λMax 234nm

VALIDATION[2, 5, 6, 7, 8, 9]

The proposed method was validated according to ICH (Q2) R1 guidelines for validation of analytical procedures. As per the ICH guidelines, the method validation parameters checked were Selectivity, linearity, precision and accuracy.

Selectivity:
The selectivity of the method was assessed by analyzing standard drug, and pharmaceutical product, comparing the maxima and minima of the standard with that of the sample to determine whether the pharmaceutical product and excipient lead to interfere in the estimation.

Limit of Detection and Limit of Quantification:
The Limit of Detection (LOD) is the smallest concentration of the analyte that gives the measurable response. LOD was calculated using the following formula
LOD = 3.3 σ /S

The Limit of Quantification (LOQ) is the smallest concentration of the analyte, which gives response that can be accurately quantified. LOQ was calculated using the following formula
LOQ = 10 σ/S

Where, σ is standard deviation of the response and
S is the slope of the calibration curve.
LOD& LOQ of Acebutolol hydrochloride was found to be 0.2670µg/ml & 0.8091µg/ml respectively.

Linearity:
Different volumes of stock solutions were suitably diluted with corresponding medium (

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2,4,6,8, and 10 µg/ml) to get the desired concentrations. Each solution was analyzed in triplicate. The amplitude values were plotted against the corresponding concentrations to obtain the linear calibration curve[10, 11, 12, 13].

S. No	Concentration of Acebutolol hydrochloride (µg/ml)	Absorbance at 233 nm (1N NaOH)	Absorbance at 234 nm (1N HCl)	Difference in absorbance
1	2	0.189	0.177	0.0120
2	4	0.283	0.259	0.0240
3	6	0.401	0.367	0.0345
4	8	0.570	0.525	0.0452
5	10	0.734	0.678	0.0561

Table 1: Linearity of Acebutolol hydrochloride by difference spectrophotometry

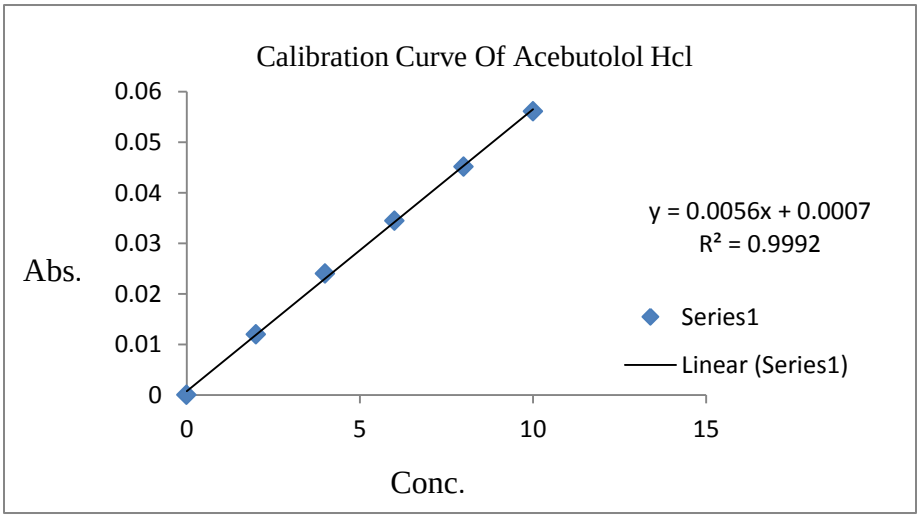

Figure-3-Showing linearity of Acebutolol

Range:
2-10 µg/ml.

Precision:
Precision of analytical methods were expressed in relative standard deviation (RSD) of a series of measurements. The intra-day and inter-day precisions of the proposed methods were determined by estimating the corresponding responses (i.e. three concentrations / three replicates each) of the sample solution on the same day and on three different days respectively. Precision was calculated as inter-day and intra-day coefficient of variation [14].

1N HCL

Drug	Conc.[µg/mL]	Trial	Trial	Trial	SD	%RSD
Acebutolol	4	0.264	0.259	0.255	0.004509	1.738785
Acebutolol	6	0.382	0.385	0.379	0.003	0.78534
Acebutolol	8	0.520	0.537	0.526	0.008622	1.633925

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1N NaoH

Drug	Conc. [µg/mL]	Trial	Trial	Trial	SD	%RSD
Acebutolol	2	0.283	0.288	0.284	0.002646	0.928334
Acebutolol	4	0.409	0.421	0.418	0.006245	1.501201
Acebutolol	8	0.513	0.524	0.527	0.007371	1.413897

Accuracy:

The accuracy of the method was determined by recovery experiments. A known amount of standard Acebutolol hydrochloride corresponding to 2, 4, 6 and 8, 10% of the label claim(standard addition method) was added to preanalysed sample of tablet. The recovery studies were carried out in triplicate at each level [15].

Standard concentration [µg/mL]	Difference in Abs $\times 10^2$	found concentration [µg/mL]	Recovery %
2	0.012	2.017857	100.8929
4	0.024	4.160714	104.0179
6	0.0345	6.035714	100.5952
8	0.0452	7.946429	99.33036
10	0.0561	9.892857	98.92857

RESULT AND DISCUSSION

The optical characteristics such as Beer's law limits, percent relative standard deviation and percent range of error were found to be within the limit and satisfactory. All of the analytical validation parameter for the proposed method was determined according to ICH guidelines. The method was found to provide high degree of precision and reproducibility.

The recovery studies showed that the result were within the limit indicating no interference. The proposed method is simple, sensitive, accurate and precise and can be successfully employed for the routine analysis of the Acebutolol hydrochloride in bulk drug.

CONCLUSION

The proposed method is simple, accurate, precise and selective for the estimation of Acebutolol hydrochloride in bulk drug. The method is economical, rapid and do not require any sophisticated instruments contrast to chromatographic method.it can be effectively applied for the routine analysis of Acebutolol hydrochloride in bulk drug.

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