Research Article **ISSN: 2349 – 7106**

Asian Journal of Research in Chemistry and Pharmaceutical Sciences

Journal home page: www.ajrcps.com

https://doi.org/10.36673/AJRCPS.2020.v08.i01.A09

DEVELOPMENT AND VALIDATION OF SPECTROPHOTOMETRIC METHOD FOR THE DETECTION OF SALBUTAMOL SULPHATE IN PURE DRUG AND PHARMACEUTICAL DOSAGE FORM

R. M. Chilka*[1], K. A. Kamalapurkar[1], S. N. Patil[1]

[1*]Department of Pharmaceutics, Faculty of Pharmacy, D.S.T.S. Mandal's College of Pharmacy, Solapur-413004, Maharashtra, India.

ABSTRACT

Objective: A new, easy, non-complex, appropriate and re-performable analytical method was developed for the determination of Salbutamol Sulphate pure drug. **Methods:** The analysis was performed at λ_{max} 280nm using Di Methyl Formamide (DMF) as blank/diluent. According to International Conference on Harmonization (ICH) the method was validated by the following the analytical performance parameters which included accuracy, precision, linearity, LOD, LOQ, Ruggedness and Robustness. **Results:** The drug follows the Beer's Lambert's law in a concentration range of 10-50µg/ml with regression equation y = 0.0096x-0.0541 and regression co-relation coefficient of 0.9986. However, the method was found to be extreme sensitive with LOD (2.365µg/ml) and LOQ (7.167µg/ml). **Conclusion:** Depending on results the above method can be performed successfully for the determination of Salbutamol Sulphate pure drug.

KEYWORDS

Salbutamol Sulphate, Analytical method, Spectrophotometry, Di Methyl Formamide (DMF), Method development and Validation.

Author for Correspondence:

Chilka R. M,
Department of Pharmaceutics,
D.S.T.S. Mandal's College of Pharmacy,
Solapur, Maharashtra, India.

Email: revatichilka@gmail.com

INTRODUCTON

Asthma is an inflammatory disease of airways to lungs. It causes breathing difficulty and further leads to chronic bronchitis, chronic obstructive pulmonary disorder (COPD)[1].

Salbutamol is a short-acting, selective beta2-adrenergic receptor agonist useful in the treatment of asthma and COPD. It is more selective for beta2 receptors than beta1 receptors giving it higher specificity towards pulmonary beta receptors than beta1-adrenergic receptors which is located in the

heart. Salbutamol is mostly used for acute episodes of bronchospasm caused by chronic bronchitis, bronchial asthma and other chronic bronchopulmonary disorders such as chronic obstructive pulmonary disorder (COPD). It is also used prophylactic ally for exercise-induced asthma.

The receptor mainly inhibits the phosphorylation of myosin and lowers intracellular ionic calcium concentrations, which results in relaxation. In 1982 Salbutamol Sulphate was approved for medical use in the United States. In the list of World Health Organization of Essentials Medicines, it is present[1].

Structure of Salbutamol Sulphate

The chemical name of Salbutamol Sulphate is 4-[2-(tert-butylamino)-1-hydroxyethyl]-2-(hydroxymethyl) phenol; sulfuric acid. It has molecular formula of $C_{13}H_{23}NO_7S$ and molecular weight of 337.39gm/mol. Salbutamol Sulphate is White powder and has melting point 180ºC. The drug is soluble in ethanol and partially soluble in water[2].

The aim of this work is to introduce to a simple, easy and non complex method to determine the pure drug.

MATERIAL AND METHODS

The solvent was selected based on solubility of the drug. The solvent such as water, ethanol, methanol, chloroform, acetonitrile, n-hexane, DMSO, DMF. Salbutamol is soluble in ethanol, chloroform, DMSO and DMF. In this method the UV- Visible spectrophotometer (SYSTRONIC 2201 model). The UV- VISIBLE Spectrophotometer shows a resolution of 1nm with matched quartz cuvettes of 1cm path length. The weight was taken on analytical balance. Sonicator was used to dissolving Salbutamol Sulphate in DMF. The pure drug is taken as a gift sample. All the chemicals were used of laboratory grade. Dilutions of Salbutamol Sulphate were from the stock solution (1000µg). The dilutions of Salbutamol Sulphate were scanned over a range of 200-400nm by using UV- Visible Spectrometer. The observations were showed by the drug, maximum absorbance at 280nm, which was selected as wavelength for detection.

Preparation of Standard drug solution

10mg of Salbutamol Sulphate pure drug was weighed accurately on an analytical balance and transferred into a 10ml volumetric flask and the volume was made up to the mark with Di Methyl Formamide to get the stock solution (1000µg/ml).

Preparation of Calibration curve

To a series of 10ml volumetric flask, 0.1-0.5ml of standard stock solution was pipette out separately. The volume was adjusted using DMF. The solutions were measured at wavelength of 280nm against blank solution.

RESULTS AND DISCUSSION[3-12]

The method was validated as per ICH guidelines which are as follows,

Linearity

The linearity was performed by taking aliquots of concentration of 10-50µg/ml and absorbance was measured. It was performed in single day only. The obtained absorbance shows approximate correlation coefficient at wavelength 280nm. The slope and intercept values were recorded. The linearity was plotted against absorbance of Salbutamol Sulphate vs concentration of Salbutamol Sulphate.

Accuracy

The accuracy is a parameter of an analytical method in UV-Visible Spectrophotometer which gives the approximate results obtained by that method to the theoretical value. The standard addition method is used to analyze accuracy which was performed by using priorly analyzed standard solutions. The percentage relative standard deviation and percentage recovery were analyzed by using standard solution.

Range

The range is the parameter of analytical method. It is an interval between lower and upper concentration limit of an analyte i.e. 10-50µg/ml.

Precision

The precision is performed as intra-day and inter-day. Intra-day precision was performed in one day and inter-day was performed in three days. At 30µg/ml the Salbutamol Sulphate was evaluated.

Limit of Detection (LOD)

The lower limit of detection or it is also called as limit of detection (LOD). The lowest quantity of substance that can be able to distinguish from the absence of that substance with a stated experimental level.

LOD = 3.3* standard deviation / slope.

Limit of Quantitation (LOQ)

The limit of quantitation (LOQ) is the lowest concentration of analyte. In which a method or measurement system performance is acceptable for a specific use.

LOQ = 10* standard deviation / slope

Ruggedness

Ruggedness is defined as the reproducibility of test results when the method is performed under actual use conditions like different analyst, laboratories, columns, instruments, sources of reagents, chemicals, solvents etc. This study shown that there is no any influence of these conditions on test results.

Robustness

Robustness is defined as a measure of its capacity to remain unaffected by small, but deliberate variations in method parameters. The aspect of robustness is to develop methods that allow for expected variations in the separation parameters.

Linearity

Salbutamol Sulphates Five different concentrations were prepared and analyzed. The wavelength was found to be 280nm. The correlation coefficient was found to be 0. 998. The absorbance was found in range 0-1. Therefore, the analyzed parameter was found to be validated (Table No.1).

Precision

Intra-day Precision

Intra-day precision was found within limit i.e. 30µg/ml at 280nm. The relative standard deviation is less than 2%. Therefore, the parameter was found to be validated (Table No.3).

Inter-day precision

Inter-day precision was performed in three days and the obtained results of concentration 30µg/ml at 280nm shown. The relative standard deviation is less than 2%. Therefore, the performed parameter was found to be validated (Table No.4).

Limit of detection

The limit of detection was found to be 2.365µg/ml (Table No.2).

Limit of quantitation

The limit of quantitation was found to be 7.167µg/ml (Table No.2).

Ruggedness

The change in analyst at concentration of 20µg/ml shown that the obtained result does not affected by it (Table No.5).

Robustness

The change in concentration i.e. 25µg/ml and change in wavelength i.e. at 280nm and 284nm. The obtained results shown that there is negligible effect on results. The robustness was found in limit i.e. the relative standard deviation is less than 2%. Therefore, the performed parameter was found to be validated (Table No.6).

Table No.1: Results for linearity

S.No	Concentration (µg/ml)	Absorbance
1	10	0.043
2	20	0.142
3	30	0.232
4	40	0.323
5	50	0.434

Table No.2: Regression analysis of the calibration curve for developed method

S.No	Parameters	Method values
1	λ max	280nm
2	Beer's law	10-50µg/ml
3	Correlation coefficient	0.9986
4	Regression equation (Y= mx + c)	0.0096x-0.0541
5	Slope (m)	0.0096
6	Intercept (c)	0.0541
7	LOD (µg/ml)	20365
8	LOQ (µg/ml)	7.167

Table No.3: Intra-day results of Precision

S.No	Concentration (µg/ml)	Absorbance 1	Absorbance2	Absorbance3	%RSD
1	30	0.232	0.228	0.234	
2	30	0.231	0.227	0.233	
3	30	0.232	0.232	0.2236	
4	30	0.233	0.236	0.232	
5	30	0.232	0.234	0.233	
6	30	0.228	0.234	0.234	
%RSD	-	0.75699859	1.553239025	1.722792517	1.344343

Table No.4: Inter-day results of Precision

S.No	Concentration (µg/ml)	Absorbance 1	Absorbance2	Absorbance3	%RSD
1	30	0.232	0.231	0.232	
2	30	0.231	0.234	0.234	
3	30	0.232	0.232	0.234	
4	30	0.233	0.233	0.232	
5	30	0.232	0.232	0.233	
6	30	0.228	0.230	0.231	
%RSD	-	0.75699859	0.609575	0.520512955	0.629029

Table No.5: Result of Ruggedness

S.No	Concentration	Analyst 1	Analyst 2
1	20µg/ml	0.142	0.143
2	-	0.141	0.142
3	-	0.143	0.139
4	-	0.142	0.142
5	-	0.139	0.142
6	-	0.142	0.141
7	Average	0.1415	0.1415
8	SD	0.0013784	0.0013784

Table No.6: Result of Robustness

Wavelength	280nm	284nm
Concentration	25µglml	25µg/ml
Absorbance	0.185	0.186
	0.184	0.185
	0.186	0.184
	0.187	0.186
	0.185	0.185
	0.184	0.185
Average	0.18516667	0.18516667
SD	0.00116905	0.00075277

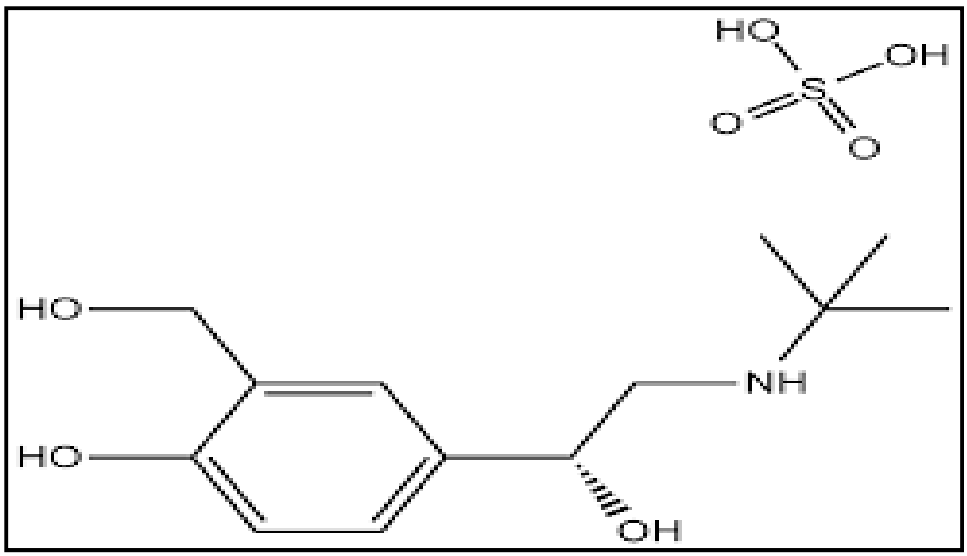

Figure No.1: Structure of Salbutamol sulphate

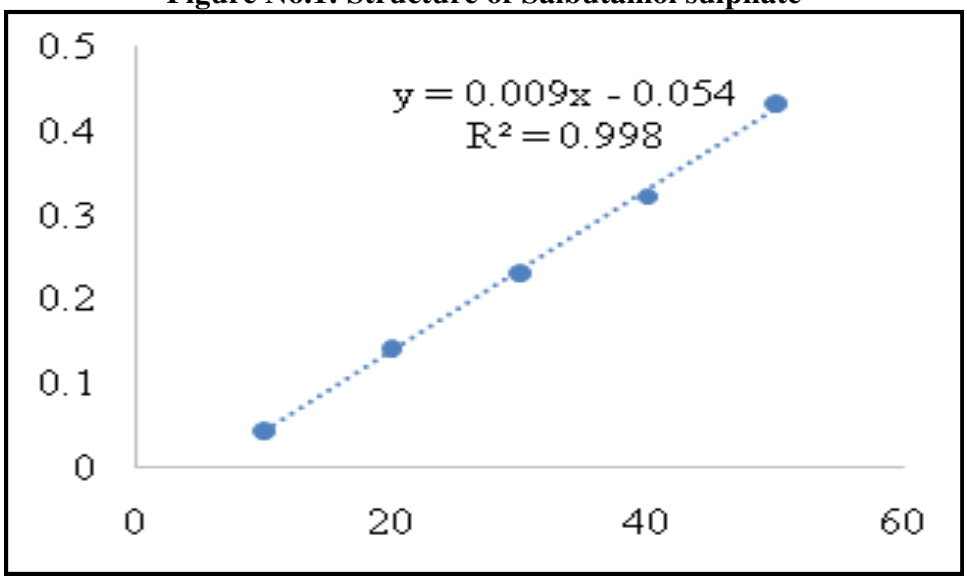

Figure No.2: Calibration curve of Salbutamol sulphate

CONCLUSION

The analytical method was developed and validated thoroughly for quantitive determination of Salbutamol Sulfate as a pure drug. The developed method was found to be simple, non complex, easy, appropriate, precise and reproducible.

ACKNOWLEDGEMENT

Authors are thankful to the principal, D. S. T. S. Mandal's College of Pharmacy, Solapur, for providing the necessary facilities.

CONFLICT OF INTEREST

We declare that we have no conflict of interest.

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Please cite this article in press as: Chilka R M *et al*. Development and validation of spectrophotometric method for the detection of salbutamol sulphate in pure drug and pharmaceutical dosage form, *Asian Journal of Research in Chemistry and Pharmaceutical Sciences,* 8(1), 2020, 57-62.