METHOD DEVELOPMENT AND VALIDATION OF CITALOPRAM HYDROBROMIDE IN BULK AND TABLET DOSAGE FORM BY UV-SPECTROSCOPY

Mr. M. Sivaganesh

Assistant professor, Department of pharmaceutical analysis, Arunai college of Pharmacy,Thiruvannamalai, Tamilnadu. E-Mail Id: sivaganesh2761@gmail.com

Dr. S.K. Senthilkumar

Professor, Principal&Head, Department of Pharmaceutics, Arunai college of Pharmacy, Thiruvannamalai, Tamilnadu. E-Mail Id: senthilmekala@gmail.com

Mr. S.Vetrivel

Arunai college of Pharmacy, Thiruvannamalai, Tamilnadu.

E-Mail Id: vetri122002@gmail.com

Mr. S. Vignesh kumar

Arunai college of Pharmacy,Thiruvannamalai, Tamilnadu.

E-Mail Id: vigneshkumar2432@gmail.com

Mr. E.Vikram

Arunai college of Pharmacy,Thiruvannamalai, Tamilnadu.

E-Mail Id: aalaporantamizhan44@gmail.com

Miss. V. Vinothini

Arunai college of Pharmacy,Thiruvannamalai, Tamilnadu.

E-Mail Id: vinolakshmi21@gmail.com

Miss. R. Yamuna

Arunai college of Pharmacy,Thiruvannamalai, Tamilnadu.

E-Mail Id:yy9243127@gmail.com

Corroesponding Author

Mr. M. Sivaganesh**,** *Assistant professor, Department of pharmaceutical analysis, Arunai college of Pharmacy,Thiruvannamalai, Tamilnadu.*

Abstract:

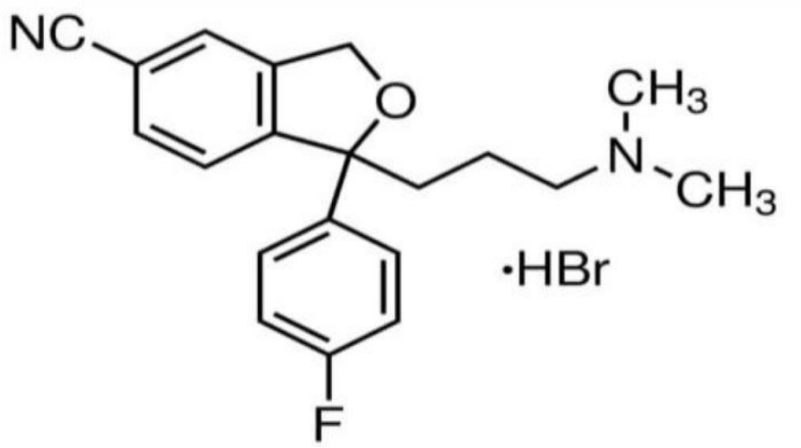
INTRODUCTION: Citalopram hydrobromide is a selective serotonin reuptake inhibitor (SSRI) that is taken orally and has a chemical structure distinct from other SSRIs, tricyclic, tetracyclic, and other antidepressant medications. Citalopram HBr, also known as (3-dimethylaminopropyl)-1-(4-fluorophenyl)-1,3-dihydroisobenzofuran-5 carbonitrile HBr. It is a racemic bicyclic phthalate derivative. The molecular weight is 405.35, and the formula is C20H22BrFN2O. The natural form of citalopram HBr is a fine, white to off- white powder. Citalopram HBr is only weakly soluble in ethanol, chloroform, and water.. OBJECTIVES: Develop and validate a simple, rapid, accurate, economic and precise UV/VIS method for Citalopram HBr in bulk and tablets formulation. METHODOLOGY: Choices of a common solvent were essential so various solvent ranges including Chloroform, Methanol, Distilled Water, Diethyl Ether and Conc. HCl were analysed. CONCLUSION: Among different solvents chloroform has showed better result, hence chloroform was selected as a solvent for the proposed method. Citalopram Hydrobromide showed maximum absorbance at 243 nm. The percentage recoveries for Citalopram Hydrobromide were found in the range of 99- 100 %. Method was quantitatively evaluated in terms of linearity, accuracy, precision, robustness, ruggedness and recovery. The method was simple, convenient and suitable for the determination of Citalopram Hydrobromide from bulk and tablet dosage form.

Key words: Citalopram Hydrobromide, UV-Spectrophotometry, Tablets.

INTRODUCTION

Citalopram hydrobromide is a selective serotonin reuptake inhibitor (SSRI) that is taken orally and has a chemical structure distinct from other SSRIs, tricyclic, tetracyclic, and other antidepressant medications. Citalopram HBr, also known as ()-1-(3-dimethylaminopropyl)-1-(4-fluorophenyl)-1,3-dihydroisobenzofuran-5 carbonitrile HBr. It is a racemic bicyclic phthalate derivative. The molecular weight is 405.35, and the formula is C20H22BrFN2O. The natural form of citalopram HBr is a fine, white to off- white powder. Citalopram HBr is only weakly soluble in ethanol, chloroform, and water..

STRUCTURE



Citalopram hydrobromide, which affects the central nervous system by blocking the selective serotonin reuptake inhibitors, is used to treat adult depression. It is a quantitative technique for determining how much a chemical compound absorbs light by UV-visible spectroscopy. By contrasting the amount of light that travels through a sample that which passes through a reference sample or a blank, this is achieved. The objective of the current study was to create a rapid, reliable, cost-effective, exact, and durable UV method of Citalopram hydrobromide for calculating bulk and tablet dosage form. Chloroform was used as the solvent.

MATERIALS AND METHOD

Instrument:

A Shimadzu UV-1800 240V UV/VISIBLE spectrophotometer was used having two matched 1 cm matches quartz cell.

Chemical and reagents:

All the reagents and solvents were of analytical grade such as Chloroform, Methanol, Conc.HCL, Distilled water, Diethyl ether was obtained from Millipore,Citalopram hydrobromide was gifted from Medrich pharma Pvt Ltd, Bangalore.

Preparation of Standard Stock Solution:

Accurately weighing 10 mg of Citalopram HBr, it was then transferred to a 10 ml volumetric flask.To completely dissolve it, 10 ml of chloroform were added and Sonicated. Then, using the same solvent and make up the volume upto 10ml. The resulting concentration was 1000 µg/ml. Chloroform was used to further dilute the standard stock solution to 100 µg/ml. To achieve a concentration of 10 µg/ml, the same solvent has been used for dilution once more and make up the volume upto 10 ml. Using the same solvent, a final dilution was performed to get a concentration of 1 µg/ml. Between 200 and 400 nm, the solution was scanned against a blank. The UV wavelength at which Citalopram is most readily absorbed is 243 nm.

Preparation of sample solution:

Accurately weighed 10 tablet of Citalopram hydrobromide (Mahapram 20 mg) and calculated the average weight. Then the tablet were powder. The tablet powder equivalent to 11.5mg was measured and transferred into 10ml standard flask. Then the volume was made up to 10ml with Chloroform, to get the concentration 1150µg/ml. From this,1ml was pipetted out and transferred into a 10 ml volumetric flask and make up the volume upto 10 ml with the same solvent to get the concentration 115µg/ml. Again this, 1ml was pipetted out and transferred into 10 ml volumetric flask and make upto 10 ml with the same solvent to get the concentration 11.5µg/ml. Again this, 1ml was pipetted out and transferred into 10ml volumetric flask and make upto 10 ml with the same solvent to get the concentration 1.15 µg/ml. Both the sample and standard solutions absorbance were measured at 243 nm against blank. The percentage purity was calculated by using the following formula,

Amount of Citalopram in each tablet was calculated by using following formula,

$$\frac{AT}{AS} \times \frac{WS}{DS} \times \frac{DT}{WT} \times \frac{P}{100} \times \frac{Average\ Weight}{Label\ claim} \times 100$$

Where,

AT = Absorbance of Citalopram obtained with test preparation.

AS= Absorbance of Citalopram obtained with standard preparation.

WS= Weight of working standard taken in mg

WT= Weight of sample taken in mg

DS= Dilution of standard solution

DT= Dilution of sample solution

P = Percentage purity of working standard

Method validation:

The method was developed and validated according to the analytical procedure as per the ICH guidelines for validation of analytical procedures in order to determine linearity, accuracy precision, LOD, LOQ, robustness, ruggedness.

Linearity:

The linearity was evaluated by analysing the different concentration of the standard solution of Citalopram HBr. The Beer-Lambert's concentration range was found to be 2-10 µg/ml for Citalopram HBr respectively. The linearity of the relationship between absorbances and concentration was determined by plotting the calibration curves for Citalopram HBr are shown in Figure 2 and Table 3.

Accuracy (% Recovery):

The accuracy study was done by using the standard addition method. 11.5 mg of citalopram HBr tablet powder is added with the pre -quantified 6µg/ml sample solution of citalopram HBr were spiked with an extra 50,100 &150 % of the standard citalopram HBr. At 243nm, absorbance were measured and drug concentration was determined. The developed method was used to examine these mixures. Three times the experiment was conducted. At each concentration level, the percentage RSD, the percentage recovery of the samples, and the percentage were determined and are displayed in Table 6

Precision:

Repeatability measurement was carried out by analyzing six different solutions containing same concentration 4 µg/ ml Citalopram HBr and % RSD was calculated. Repeatability of the method was established by analyzing various replicates samples of Citalopram HBr. Precision was carried out by performing interday and intraday variation. In Inter day variation the sample was analyzed on different days. In an intraday variation in the absorbance was measured three times in a day. Inter and intraday precision was determined using concentration 4µg/ml.

Intraday Precision:

In the intraday variation study was determined for a solution (4µg/ml) and was analyzed within a days (i.e. morning, afternoon, evening). Mean, standard deviation and % RSD was calculated and shown in Table 4.

Interday Precision:

In the inter day variation study was determined for a solution (4µg/ml) and was analyzed three times for the consecutive days. Mean, standard deviation and % RSD was calculated and shown in Table 5.

Ruggedness:

The ruggedness of the proposed method was evaluated by applying the developed procedure to assay of 1 µg /ml of citalopram using the same instrument by two different analyst under the same optimized conditions at different days. The results are shown in table 7.

Robustness:

The robustness of the method was determined by introducing small changes in UV parameter such as changing in the wavelength. The results are shown in table 8.

METHOD DEVELOPMENT OF UV-SPECTROSCOPY:

S.No	Wavelength in nm	Absorbance
1	238	0.102
2	239	0.105
3	240	0.107
4	241	0.110
5	242	0.112
6	**243**	**0.114**
7	244	0.111
8	245	0.108
9	246	0.107
10	247	0.105

Table-1

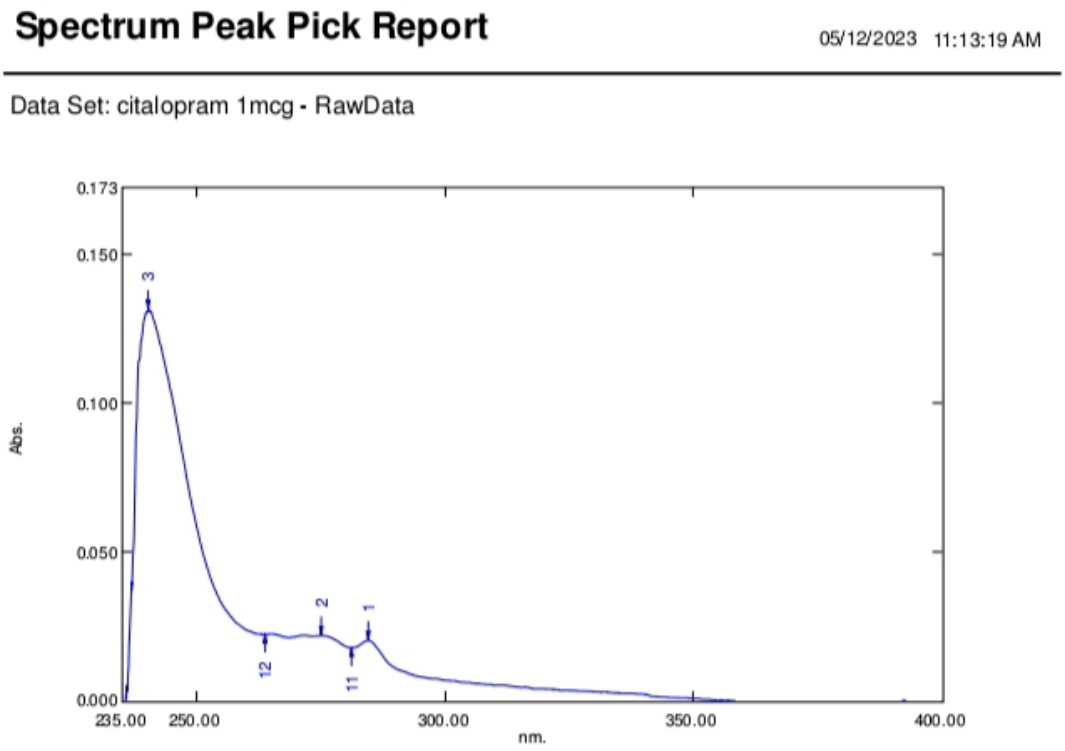


Figure-1

DETERMINATION OF PERCENTAGE PURITY :

S.NO	Standard absorbance	Sample absorbance	Percentage purity	Average % purity	SD	% RSD
1	0.114	0.132	99.30	99.89	0.7284	0.7292
2	0.113	0.130	99.17			
3	0.114	0.131	100			
4	0.117	0.132	101			
5	0.120	0.137	100			

Table-2

UV METHOD VALIDATION:

LINEARITY

S.No	Concentration (µg/ml)	Average absorbance	Correlation co efficient	LOD	LOQ	Slope	Intercept
1	2	0.164	0.9998	0.3822	1.1584	0.0442	-0.0765
2	4	0.252					
3	6	0.344					
4	8	0.431					
5	10	0.516					

Table-3

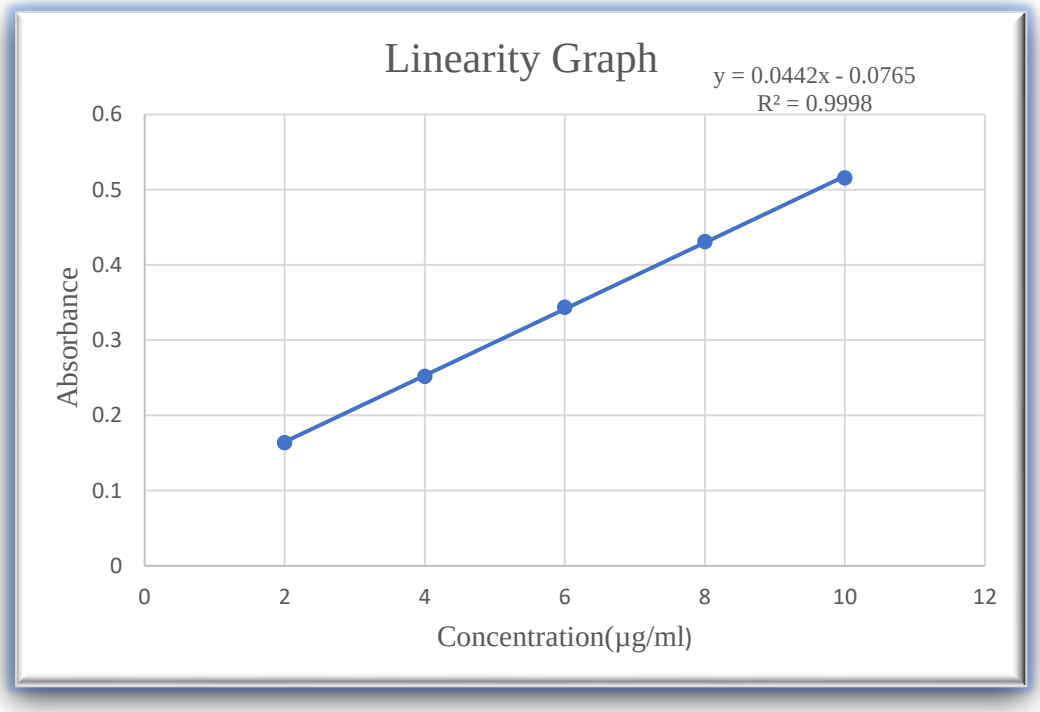


Figure-2

Precision:

Intraday precision:

S.NO	Absorbance	Average	SD	% RSD
1	0.225	0.2215	0.003987	1.8
2	0.224			
3	0.215			
4	0.219			
5	0.225			

Table-4

Interday precision

S.NO	Absorbance	Average	SD	% RSD
1	0.220	0.2225	0.003082	1.3
2	0.223			
3	0.221			
4	0.225			
5	0.219			

Table-5

Recovery Study of Citalopram HBr by UV method

S.No	% Concentration	Average Absorbance	Amount Added (mg)	Amount Found (mg)	% Recovery	Mean Recovery	SD	% RSD
1	50%	0.298	4.99	5.1	97.84%	90.80	1.036	1.049
2	100%	0.208	9.99	10.0	99.9%			
3	150%	0.257	14.9	15.1	98.67%			

Table-6

Ruggedness:

The ruggedness of the proposed method was evaluated by applying the developed procedure to assay of 1 µg /ml of citalopram using the same instrument by two different analyst under the same optimized conditions at different days. The obtained result were found to reproducible, since there was no significant difference between analysts. Thus the proposed method considered could be rugged. The results are shown in table-7.

S.No	Analysts	Coc. (g/ml)	Absorbance	Standard Deviation	%RSD
1	Analyst-1	1	0.131	0.00130	0.99
		1	0.130		
		1	0.133		
		1	0.132		
		1	0.130		
2	Analyst-2	1	0.133	0.0019	1.43
		1	0.132		
		1	0.130		
		1	0.134		
		1	0.135		

Table-7

Robustness

The robustness of the method was determined by introducing small changes in UV parameter such as changing in the wavelength 4.The results are shown in table-8.

S.NO	Wavelength	Absorbance
1	241	0.130
2	243	0.132
3	245	0.134

Table-8

Conclusion:

The method were found to be rapid, economical, accurate and precise for the determination of Citalopram in bulk drug in tablet by UV-Spectrophotometer methods produce comparable results can be used for precise and accurate analysis of Citalopram in its pure and tablet dosage form.The values of % recovery was close to 100% indicating reproducibility and accuracy of the proposed method successfully employed as a quality control tool for the analysis of Citalopram in its tablet dosage form and in bulk drug.

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