History of Medicine Studies

ISSN:1300-669
Volume 16 Issue 2 July 2020

Spectrophotometric Method Development and Validation of Levosulpiride in Bulk and Pharmaceutical Formulations.

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Abstract

A validated UV-Visible spectrophotometer technique was used to assess the levosulpiride concentration in both bulk and pharmaceutical formulation. In 0.1 N HCl, the maximum wavelength (λmax) measured for levosulpiride was 288.1 nm. Between 6 and 36µg/ml, the medication demonstrates linearity. The standard graph showed a correlation value of 0.999. The suggested procedure produced test percentages of commercial formulations that were consistent with the claims made on the label. A recovery experiment was conducted at three distinct levels (80%, 100%, and 120% recovery) to verify the method's accuracy. The percentage recovery ranged from 98.00% to 102.00%. The method's accuracy and repeatability were confirmed by the low % RSD. Experimentation with the method's repeatability, precision, and intra- and inter-day fluctuations showed that it agreed well with %RSD. The suggested approach was determined to be strong and resilient. Levosulpiride, both in bulk and medicinal dose form, may be routinely analyzed using the aforementioned approach.

Keywords: Area under the curve, validation, levosulpiride

Introduction

The anti-psychotic Levo-isomer of sulpiride is known as levosulpiride. Peptic ulcers, anxiety problems, and schizophrenia are among the conditions that it helps alleviate. According to Figure 1, its chemical formula is 5-(aminosulfonyl)-N-[(1-ethyl-2-pyrrolidinyl)methyl]-2-methoxybenzamide. The Merck Index includes it.2) No pharmacopoeia recognizes it as an official ingredient.

By inhibiting the pre-synaptic dopamine synthesis and release, levosulpiride acts as a D2-dopamine antagonist, which, at low dosages, enhances the dopaminergic neurotransmission.(3) Functional dyspepsia, psychosis, and depression are common indications for its prescription. Tonini et al. tested the racemic activity and found that the Levo version was more active. Levosulpiride toxicity was investigated by Lozano et al.(5) The UV Spectrophotometric and RP-HPLC methods for estimating levosulpiride in both bulk drug and formulation were established by Silambaresan et al.(6) It is the aim of this research to provide analytical techniques for the bulk and formulation determination of levosulpiride that are easy to use, sensitive, accurate, economical, and specific.

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ISSN:1300-669
Volume 16 Issue 2 July 2020

MaterialsandMethods

Sun Pharmaceuticals, Jammu, provided a free, pure sample of levosulpiride. Hydrochloric acid, sodium hydroxide, and methanol are the chemicals utilized, and they are of an analytical quality. Throughout the investigation, a UV-Visible spectrophotometer from Shimadzu, equipped with UV Probe software, was employed.

The sample container was a quartz cell with a 10-millimeter route length. We got the pills from a drugstore down the street. A precise 100 milligrams of the pure sample was dissolved in 100 milliliters of the corresponding solvents at a concentration of 1 milligram per milliliter. The appropriate solvents were used to create a stock solution of Levosulpiride at a concentration of 100 µg/ml. Twenty precisely measured and powdered tablets containing 100 mg of levosulpiride equivalent were used in the investigation. Volumes were prepared with the appropriate solvents from aliquots of stock solutions transferred to a series of 10 ml standard flasks for the manufacture of varied concentrations. Levosulpiride in 0.1 N HCl was made at five different concentrations ranging from 20 to 100 µg/ml. Spectroscopy was used to scan the fluid from 400 nm to 200 nm.

In order to determine if a standard solution has a wide or not sharp peak, we may utilize the area under curve (AUC) approach using a UV visible spectrophotometer. The plotted area beneath the peak is a function of concentration and is computed in square millimeters. That is why λ1 and λ2 are chosen as the two wavelengths. The area under the curve may be determined using area computation software within the specified wavelength range. Repeated scanning yields the area for various standard concentrations, which are then plotted against their corresponding concentrations to produce a linear graph. The concentration (20-100µg/mL) and Area Under the curve (AUC) in the chosen wavelength range were plotted to create a calibration curve.(7)

Validation of the proposed method: The proposed method was validated in terms of linearity, accuracy, precisionand ruggedness.

Linearity study: Stock Levosulpiride solution in 0.1N HCl were transferred into series of 10 ml volumetric flasksand the volume was made up to the mark with water to get concentrations 20,40,60,80,100µg/ml, respectively. Thesolutions were scanned on spectrometer in the UV range 200-400 nm. The two wavelengths 220 and 288 nm wasselected for the determination of Area under Curve (Fig. 2). The calibration plot was constructed as a function ofArea underCurvevs.Concentration.

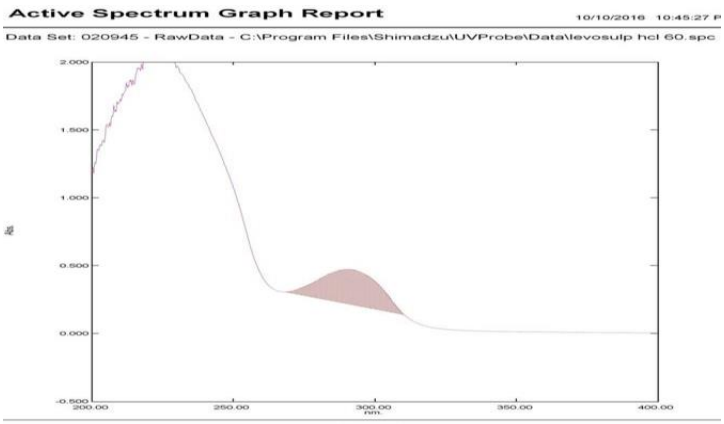

Fig. 1: Area underCurveSpectrumofLevosulpiridein0.1 NHCl

Accuracy: A known amount of standard stock solutionwas mixed with the pre -analysed sample at differentlevels(80%,100%,120%).Thesolutionswerer eanalyzedusingtheproposedmethod.

Precision: The precision was checked for inter-day andintra-day variation. Intra-day precision was determinedby analyzing the 60, 80 and 100µg/ml of drug solutionsfor three times on the same day Inter-day precision ofthe proposed method was checked by analyzing the 60,80 and 100µg/ml of Levosulpiride for three differentdays.

Sensitivity: The sensitivity of the proposed method forthe measurements of Levosulpiride was estimated byusingLimitOfDetection(LOD)andLimitofQuantifi cation(LOQ).TheLOQandLODwerecalculatedusinge quationLOD=3.3xN/BandLOQ=10xN/B,where Nisstandarddeviationof thepeak areas of the drugs(n=3), taken as a measure ofnoise, and B istheslopeofthestandardcurve.

Repeatability: On analyzing 40µg/ml concentration ofLevosulpiride solution for six times repeatability of thismethodwasestablished.

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Ruggedness: The determination of Ruggedness of theproposed method was studied by analyzing 40µg/ml ofdrug by two analysts under the similar environmentaland operationalconditions.

DeterminationofLevosulprideinBulk

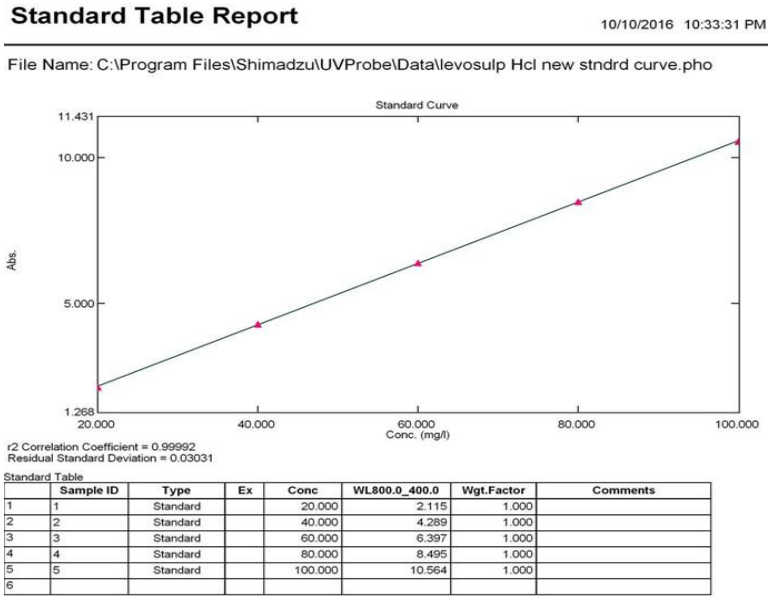
100mg of Levosulpiride was weighed accurately andtransfertoa100mlvolumetricflask,dilutedthemixturewith0.1NHCl.Thewholesolutionwasfiltered through awhatmannfilter paper no: 42 Fromthe filtrate, make up a final solution of concentration of60µg/ml.TheresultingsolutionwasscannedonaspectrophotometerintheUVrange200-400nm.Theconcentrations of the drug were calculated from linearregressionequations.

Applicationofthedevelopedmethodforpharmaceuticalformulation: Foranalysisofthecommericialformulation100mgoflevosulpiridewas transferred to a 100ml volumetric flask and 50 ml 0.1NHCl was added. After ultrasonication for 15 minutes.The mixture was diluted up to the mark with 0.1 N HCl.The whole solution was filtered through a whatmannfilter paper no: 42. From filtrate correct dilution weretakeninsuchawaythatthefinalconcentrationis60µg/ml.Theconcentrationsofthedrugwerecalculatedfrom linearregressionequations.Theresulting solution was scanned on a spectrophotometerinthe UV range 200-400nm.

ResultsandDiscussion

Methodvalidation: Thedevelopedmethodwasvalidatedinaccordancewith ICHguidelines.Drugsolutions with different concentrations are prepared asper theproceduredescribed intheexperiment.

Linearity studies: The linear regression data of Areaundercurveversusconcentrationgivesalinearrelationshipattherangeof20-100µg/mlforlevosulpiride(Fig.3).Linearregressionequationwasfound to be Y= 0.10552 X+0.04080. (Table 1) with acorrelation coefficientofr^2=0.9992.



	Sample ID	Type	Ex	Conc	WL800.0_400.0	Wgt.Factor	Comments
1	1	Standard		20.000	2.115	1.000	
2	2	Standard		40.000	4.289	1.000	
3	3	Standard		60.000	6.397	1.000	
4	4	Standard		80.000	8.495	1.000	
5	5	Standard		100.000	10.564	1.000	
6							

Fig.2:Calibrationcurveoflevosulpiride

Accuracy: Recovery studies at 80,100,120% of the preanalysedsampleshowsthatthe%recoverywasbetween99-101%.(Table 2)

Precision: The precision of proposed method expressedin %RSDandthevaluewasfoundtobelessthan2.This indicatethatthemethodis preciseandcan beusedforthedetermination ofbothdrugsin formulationand shows the reproducibility of the assay. (Table 3)**Sensitivity:**TheLODandLOQwerefoundtobe0.9479 and2.8724µg, respectively(Table 4).

Repeatability: Repeatabilitywasdeterminedbyanalyzing 60 µg/ml concentration of Levosulpiride (6times) and the % RSDwas found to be less than 2(Table 5).

Ruggedness: PeakAreameasurementofsixconcentrationsofdrugshowsthatthe%RSDwasfound tobelessthan2%(Table 6).

DeterminationofLevosulprideinbulk: Theconcentrations of the drug was calculated from AreaunderCurveversusConcentrationLinearregression equations.Thepercentageamountwasfoundinbetween98.00%to102.002%(Table 7).

Application of developed method on formulations: Theconcentrationsofthedruginamarketedformulation(Nexipride) was calculated from Area underCurveversusConcentrationLinearregressionequations.Thepercentageamountwasfoundinbetween98.00%to102.002%(Table 8).

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Table1:Linearitystudies

Concentration µg/mL	Area,[a] mean±SD(n=6)	%RSD
20	2.115±0.0148	0.28
40	4.289±0.0101	0.10
60	6.397±0.0458	0.37
80	8.495±0.0438	0.20
100	10.564±0.0622	0.20

(n=no.ofestimations)

Table2: Recoverystudies

Drug	Initialamount(µg/mL)	Amount added(µg/mL)	Amountrecovered(µg/mL,n=3)	% recovered	%RSD
Levosulpiride	40	32	31.9351	99.7972	0.6526
	40	40	40.2342	100.5855	0.4855
	40	48	48.0809	100.168	0.8570

(n=no.ofestimations)

Table3:ResultsofPrecision studies

Component	Concentration (µg/mL)	Intra-dayprecision[a] (n=3)		Inter-dayprecision[a] (n=3)	
		Amt.found	%RSD	Amt.found	%RSD
Levosulpiride	40	40.0461	0.4860	39.9351	0.6526
	60	60.0809	0.8570	60.1208	0.2526
	80	80.2127	0.4192	80.1387	0.6109

[a]Averageofthreeestimation

Table4:SensitivityStudies

LOD(µg/mL)	LOQ(µg/mL)
0.9479	2.8724

Table5:RepeatabilityStudies

Sample	Amount taken(µg/mL) (n=6)	Amountfoundin[a]%	%RSD
Levosulpiride	60	99.33±0.24	0.26

[a]Averageofsixestimation

Table6: Ruggedness study

Component	Amount taken(µg/mL) (n=6)	Amountfound[a](%)		%RSD	
		AnalystI±SD	AnalystII ±SD	AnalystI	AnalystII
Levosulpiride	60	100±0.5083	100±0.7413	0.5047	0.7372

[a]Averageofsixestimation

Table7:AnalysisofLevosulpiridein bulk

Concentration inµg/mL	Amountfound(µg)	Amount foundin %
60	59.8578	99.4076
	59.5844	98.2682
	59.8891	99.5378
	59.7953	99.1471
	59.8656	99.4401
	59.7406	98.9193

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mean±SD	59.7888±0.4746	99.1200±0.4746
%RSD	0.4788	0.4788

Table8:AnalysisofLevosulpirideinformulation(Nexipride100mg,sunpharma)

Concentration(µg/mL)	Amountfound(µg)	Amountfound(%)
60	59.8578	99.4076
	59.7797	99.0820
	59.8109	99.2122
	59.8422	99.3424
	59.8344	99.3099
	59.8188	99.2488
mean±SD	59.8240 ±0.110	99.2665 ±0.1140
%RSD	0.1149	0.1149

Conclusion

Simple, accurate, sensitive, and repeatable—those are the hallmarks of the UV Spectrophotometric approach. Using this procedure, the amount of levosulpiride in the formulation has been measured. It is a suitable and accurate quantification approach that is used for routine quality control of compounds in bulk and formulations, according to the validation procedure.

Acknowledgements

TheAuthorsaregratefulforprovidingpureLevosulpirideasgiftsamplefromSUNPHARMA,Jammu.

Conflictofinterest: Nil

Sourceofsupport: Nil

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