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Development and Validation of UV Spectrophotometric Methods for the Estimation of Propofol in Bulk and Pharmaceutical Formulations

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Abstract
Two simple and sensitive UV Spectrophotometric methods have been developed and validated for the estimation of propofol in bulk and pharmaceutical formulations. Method A is a zero order derivative method which exhibit absorption maximum at 272 nm by using methanol as the solvent and obeyed Beer's law in the concentration range of 10 – 50 µg / ml. Method B is first order derivative method which shows good absorption at 282 nm and obeyed Beer's law in the concentration range of 10 - 50 µg / ml. The results of analysis for both the methods have been validated statistically by recovery studies and the percentage relative standard deviation for both the methods were found to be below 2%. The proposed methods are sensitive, accurate, precise and economical for the routine estimation of propofol in bulk and pharmaceutical formulations.

Keywords
Methanol Propofol, Spectrophotometric methods, Validation.

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INTRODUCTION:
Propofol is a short-acting medication that results in a decreased level of consciousness and lack of memory for events. Its uses include the starting and maintenance of general anesthesia, sedation for mechanically ventilated adults, and procedural sedation. It is also used for status epilepticus if other medications have not worked. It is given by injection into a vein. Maximum effect takes about two minutes to occur and it typically lasts five to ten minutes.[2] Common side effects include an irregular heart rate, low blood pressure, burning sensation at the site of injection, and the stopping of breathing. Other serious side effects may include seizures, infections with improper use, addiction, and propofol infusion syndrome with long-term use. It appears to be safe for using during pregnancy but has not been well studied in this group. However, it is not recommended during cesarean section. Propofol is not a pain medication, so opioids such as morphine may also be used.[3] Propofol

is believed to work at least partly via a receptor for GABA.[2]

On literature survey it was revealed that several HPLC, Gas chromatography and GC/MS methods have been developed for the estimation of propofol in blood, plasma and urine samples [4,5]. HPLC method for the estimation of the same has been developed by comparison with different extraction methods also [6-9]. Since no method has been found for the estimation of propofol in bulk and pharmaceutical formulation, here an attempt has been made to develop and validate simple, sensitive and precise UV Spectrophotometric methods for the estimation of propofol in pure form and in formulation forms.

MATERIAL AND METHODS:

INSTRUMENT USED

A double beam UV-VIS spectrophotometer (UV-1800, Shimadzu) connected to computer loaded with spectra manager software UV probe 4.21 with 10mm quartz cells was used. The spectra were obtained with the instrumental parameters as follows: wavelength range:200-400nm. All weights were taken on electronic balance (Model Shimadzu AUX 120).

PREPARATION OF STNADARD STOCK SOLUTION

Propofol (100mg) was accurately weighed and transferred in a 100ml volumetric flask. Methanol (AR Grade) was added to obtain a concentration of 1000µg/ml (Stock-I). From Stock-I 10 ml of solution was withdrawn and transferred to a 100ml volumetric flask and made up the volume with methanol to obtain a concentration of 100µg/ml (Stock-II). From this stock solution-II aliquots of 1ml, 2ml, 3ml, 4ml, and 5ml were withdrawn and transferred into 10 ml volumetric flasks and made up the volume with methanol to obtain a concentration of 10µg/ml, 20µg/ml, 30µg/ml, 40µg/ml, and 50µg/ml respectively.

DETERMINATION OF ABSORBANCE MAXIMUM.

Procedure for Method A (Zero Order Derivative)

Propofol 10-50 µg/ml solutions were scanned in UV spectrophotometer in the range of 200-400nm. Methanol was used as blank.

Procedure for Method B (First Order Derivative)

Propofol 10-50 µg/ml solutions were scanned in UV spectrophotometer in the range of 200-400nm using methanol as blank and the peaks were transformed to first order derivative by taking scaling factor 100 and delta lambda 4.

PROCEDURE FOR CALIBRATION CURVE

Procedure for Method A

The standard calibration curve was obtained by measuring the absorbance of Propofol solution in concentration range (10-50µg/ml) prepared from stock solutions in Methanol at 272nm. Calibration curve of Propofol was plotted with absorbance on y-axis and concentration of propofol on x-axis.

Procedure for Method B

The standard calibration was obtained by measuring the absorbance of first order derivative propofol peaks in the concentration range of (10 - 50µg/ml) prepared from stock solutions in Methanol at 282nm. Calibration curve of Propofol was plotted with absorbance on y-axis and concentration of Propofol on x-axis.

RESULTS:

Validation of Analytical Data

The methods were validated in accordance with the ICH guidelines.

Linearity: The linearity was determined by using working standard solution between 10-50µg/ml. Absorbance values of these solutions were measured at 272nm in method A and at 282nm in method B. The values of correlation coefficient for Propofol demonstrated the good relationship between absorbance and concentrations in both the methods. Therefore, the developed methods were linear in concentration range of 10-50µg/ml.

Accuracy: The accuracy of the methods was determined by calculating percent recovery of the drug by standard addition method. Percent recovery of Propofol was determined at three different level 80%, 100% and 120% of the target concentration in triplicate absorbance at wavelength 272nm for Zero order method and 282nm for first order derivative method.

Precision: Precision of the methods were demonstrated by intraday and inter day variation studies. In Intraday variation, 30µg/ml of Propofol solution was analysed six times in a day and the absorbance values were noted. From the parameters mean, Standard deviation were calculated. The acceptable limit for intraday variation should be within 2% and results shown in table 4 and 5 indicate the drug complied with the required limit.

In Interday variation studies, solution of 30µg/ml of Propofol was analysed six times for three consecutive days and absorbance values were recorded.

LOD and LOQ: Limit of detection (LOD) is the lowest amount of analyte in the sample that can be detected. Limit of Quantification (LOQ) is the lowest amount of analyte in the sample that can be quantitatively determined by suitable precision and accuracy. LOD and LOQ was determined using the following equation.

LOQ = $10\frac{s}{m}$

LOD = $3.3\frac{s}{m}$

Where s is the standard deviation of the response and m is the slope of the related calibration curve.

The LOD and LOQ were found to be 0.05666 and 1.7171 for zero order derivative method.

The LOD and LOQ were found to be 0.1373 and 0.4163 respectively for First order derivative method.

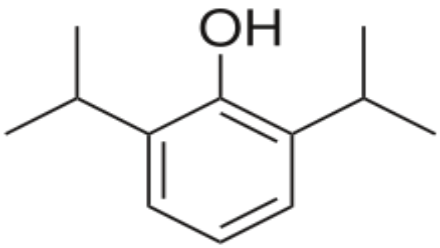

Fig. 1 Structure of Propofol

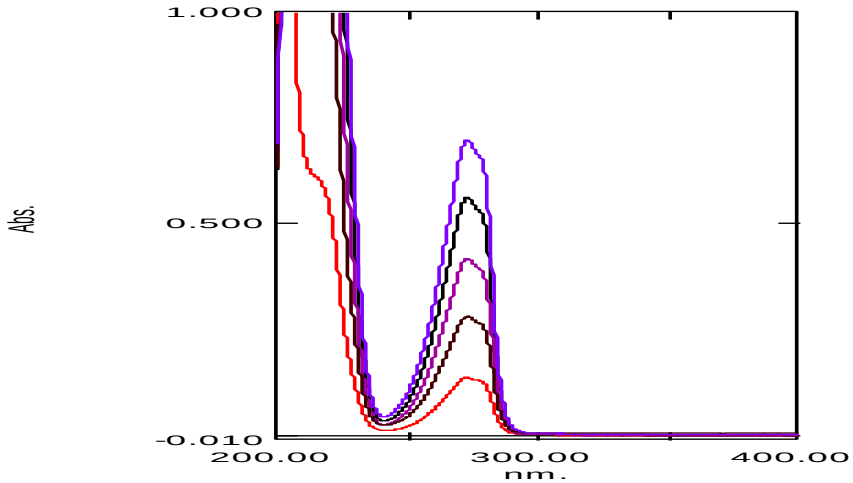

Fig. 2 Overlay spectrum of Propofol at 272 nm (Method A)

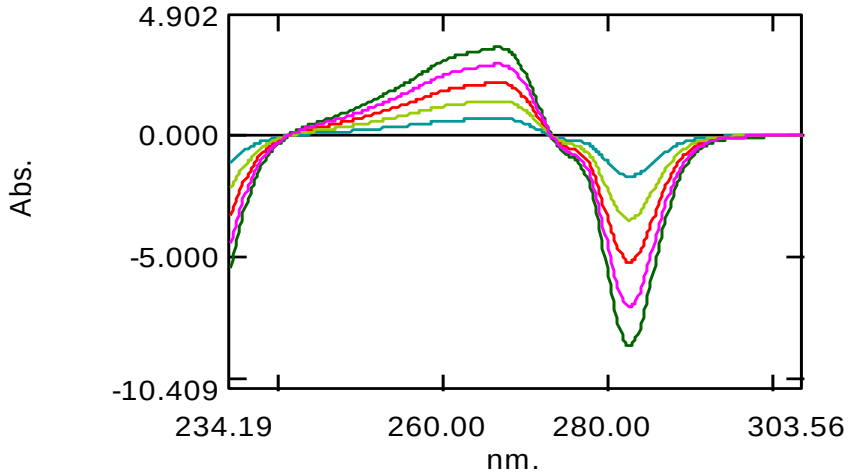

Fig. 3 Overlay spectrum of Propofol at 282 nm (Method B)

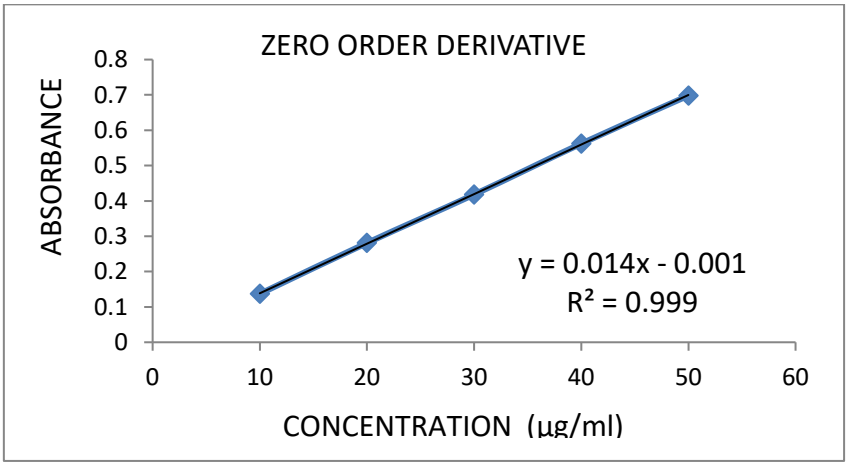

Fig. 4 Calibration curve of Propofol (Method A)

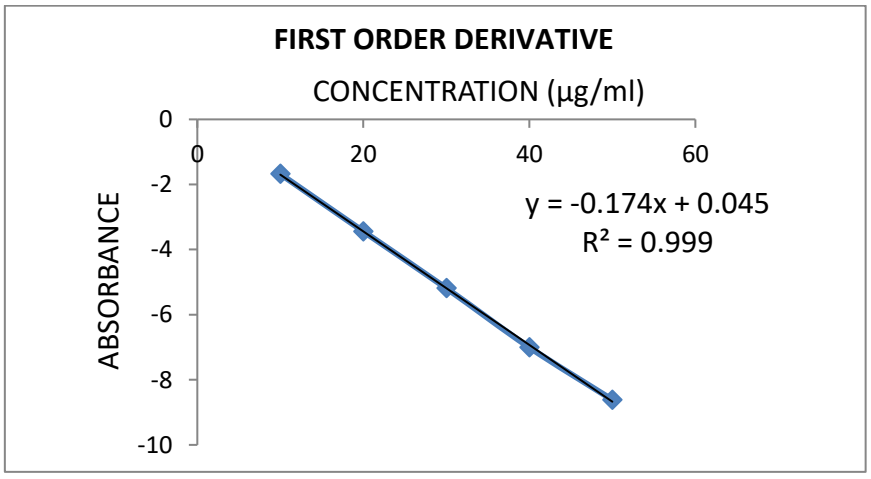

Fig. 5 Calibration curve of Propofol (Method B)

Sr No.	Concentration in µg/ml	Absorbance ± S.D in Method A at 272nm	Absorbance ± S.D in Method B at 282nm
1	10	0.137±0.0085	-1.679±0.0138
2	20	0.281±0.0051	-3.441±0.0144
3	30	0.418±0.0026	-5.188±0.0096
4	40	0.562±0.0046	-7.004±0.0106
5	50	0.698±0.0213	-8.616±0.0553

Table. 1 Linearity and Range of Method A and B.

% of Std addition	Amount of sample taken in µg/ml	Amount of standard added in µg/ml	Amount Recovered in µg/ml	% of amount recovered	% RSD
80	20	10	30.08	100.26	
100	20	20	40.06	100.15	0.07763
120	20	30	50.12	100.24	

Table. 2 Accuracy studies of Propofol by Method A

% of Std addition	Amount of sample taken in µg/ml	Amount of standard added in µg/ml	Amount Rcovered in µg/ml	% of amount recovered	% RSD
80	20	10	29.98	99.93	
100	20	20	40.03	100.07	0.08575
120	20	30	50.11	100.22	

Table. 3 Accuracy studies of Propofol by Method B

Component	Precision	Mean*	Standard Deviation*	% RSD
Propofol	Intra-day	100.038	0.1254	0.1253
	Inter-day	100.011	0.1591	0.1591

Table. 4 Intraday and Inter Day Precision for Method A

Component	Precision	Mean*	Standard Deviation*	% RSD
Propofol	Intra-day	100.016	0.1278	0.1277
	Inter-day	100.037	0.1392	0.1391

Table. 5 Intraday and Inter Day Precision for Method B

Parameter	Results Zero order method (Method A)	First order derivative (Method B)
Absorption maxima	272nm	282 nm
Beers law range	10-50 µg/ml	10-50 µg/ml
Correlation coefficient	0.999	0.999
Regression equation	Y= 0.014x-0.001	Y=-0.174x+0.045
Slope	0.014	0.174
Intercept	0.001	0.045
Accuracy	100.15-100.26%	99.93-100.22%
Precision (%RSD)	Intraday - 0.1253 Interday – 0.1591	Intraday – 0.1277 Interday – 0.1391
LOD µg/ml	0.5666	0.1373
LOQ µg/ml	1.7171	0.4163

Table 6. Summary of the methods developed. (Zero order derivative and First order derivative)

DISCUSSION:

The proposed methods provide a simple, accurate, economical and convenient methods for the analysis of Propofol using UV spectrophotometry. In method A wavelength corresponding to maximum absorbance in methanol was found at 272nm and for method B it is 282nm. Beers law was obeyed in the concentration range of 10-50 µg/ml with correlation coefficient 0.999 in both the methods. Accuracy of the proposed methods were determined by recovery studies, a good % recovery (100.15-100.26 % for Zero order method and 99.93-100.22 % for First order derivative method) of the drug obtained indicates that the methods are accurate. The methods were found to be precise as %RSD values for interday and intraday was found to be less than 2%. The limit of detection and limit of quantification of the proposed zero order method was found to be 0.5666 and 1.7171 respectively and for the First order derivative method was found to be 0.1373 and 0.4163 respectively. The results of the analysis of pharmaceutical formulation by the developed methods was consistent with the label claim, highly reproducible and reliable.

CONCLUSION:

The developed UV spectrophotometric methods for the estimation of Propofol is simple, sensitive and economical. These methods were also validated by checking the parameter such as accuracy, precision, linearity, LOD and LOQ. The proposed methods showed high level of precision as depicted by low values of standard deviation and relative standard deviation. Hence these methods can be used for routine analysis of Propofol in bulk and pharmaceutical formulations without interference of excipients and other additives.

REFERENCE:

1. www.wikipedia.com
2. Propofol: The American Society of Health-System Pharmacists, Archived from the original on 9 October 2016. Retrieved 21 January 2017.
3. Miner JR., Burton, JH: Clinical practice advisory: Emergency department procedural sedation with propofol, Annals of Emergency Medicine, 50 (2): 182–7.
4. Manoj Varchney., Christoph N. Seubert., Donn M. Dennis: A new method for the quantitation of propofol in human plasma by efficient solid-phase extraction and liquid chromatography/APCI-triple quadrupole mass spectrometry detection, Journal of Chromatography B, 810 (2) 25, October 2004, 291-296.
5. Eunyoung Han: A study of analytical methods for the determination of propofol in blood, Archives of Pharmacal Research, February 2014, 37(2),157–167.
6. Andrzej L., Dawidowicz: Determination of Propofol in Blood by HPLC. Comparison of the Extraction and Precipitation Methods, Journal of Chromatographic Science, 33 (7), 1 July 1995, 377–382.
7. G.F.Plummer: Improved method for the determination of propofol in blood by high-performance liquid chromatography with fluorescence detection, Journal of Chromatography Biomedical Sciences and Applications, 421,1987, 171-176.
8. Sónia Campos1., Joaquim Monteiro., Luís Antunes1: Simultaneous Quantification of Propofol and its Non-Conjugated Metabolites in Several Biological Matrices Using Gas Chromatography/Ion Trap – Mass Spectrometry Method, Journal of Analytical & Bioanalytical Techniques, 2014, 5,3.
9. Jae Sung Pyo : Selective and Accurate Determination Method of Propofol in Human Plasma by Mixed-Mode Cation Exchange Cartridge and GC-MS, J Anal Methods Chem, 2016, 9531769.