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Original Article

A Simple Method Development and Validation for the Determination of Tolbutamide in Bulk and Marketed Dosage Form by UV - Spectrophotometric Technique

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ABSTRACT

T*he present work was to develop simple UV spectrophotometric methods for estimation of Tolbutamide (TOL) in bulk and tablet dosage form and validate as per ICH guidelines. In this method the absorption maxima was scanned from 200 – 400 nm and the λmax was found to be 248 nm was selected for analysis of Tolbutamide. Linearity was observed in the concentration range 1-12µg/ml (r2 =0.9992) for the method. The % assay for the marketed formulation for absorption maxima and area under the curve method was found to be 100.49% and 100.78% respectively. The methods were validated with respect to linearity, precision and accuracy studies. Recovery studies for absorption maxima, and area under the curve was found to be 99.52% and 100.64% respectively. The developed methods were validated for linearity, precision, accuracy, LOD and LOQ as per ICH guidelines. The method was found to be linear within the conc. Range of 1-12µg/ml for Tolbutamide. The present method was found to be simple, linear, precise, accurate and sensitive and can be used for routine quality control analysis for the estimation of Tolbutamide in bulk and tablet dosage form.*

Keywords: *Tolbutamide (TOL), UV-Spectroscopy, Method Development, Validation and ICH guidelines.*

1. INTRODUCTION:

Tolbutamide is chemically 1-butyl-3-(4-methylphenyl) sulfonylurea [1]. It is a first-generation potassium channel blocker, sulfonylurea oral hypoglycemic medication. This drug may be used in the management of type 2 diabetes if diet alone is not effective. Tolbutamide stimulates the secretion of insulin by the pancreas [2].

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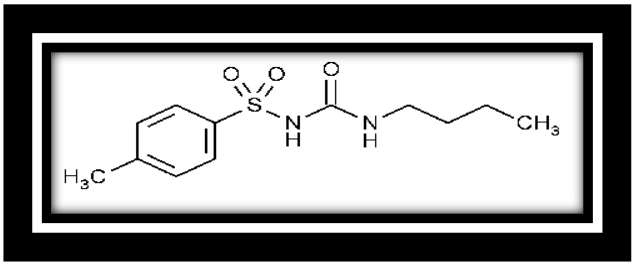

Fig. 1: Chemical structure of Tolbutamide (TOL)

Hence the method was developed and validated as per ICH guidelines [3, 4]. The literature reveals that various methods for the determination of TOL and pharmaceutical validations among these methods are UV - Spectrophotometric [5-10], HPLC method for TOL were reported [11-15].

2. MATERIALS AND METHODS

Equipment and Reagent:

An ELICO model SL210 double beam UV/Visible spectrophotometer with a matched pair of 10nm quartz cells are used for experimental purpose. Tolbutamide bulk powder was kindly gifted by KP Labs Pvt. Ltd., Hyderabad, India. The pharmaceutical dosage forms were procured from local market. Methanol (Molychem-AR grade), Distilled water (AR grade) and Whatman filter paper no. 42 (Whatman International Ltd, England) were used in study.

Preparation of standard stock solution:

Accurately weighed 10mg of Tolbutamide pure drug taken in separate 100mL volumetric flask and dissolved with 25mL of methanol and shaken for 10 min and then diluted with methanol up to mark to get 100 µg/mL standard stock solution.

Concentration of calibration curve:

Aliquots of standard stock solution were pipetted out and suitably diluted with methanol to get final concentration of 1-12 µg/mL. The solution was scanned in the spectrum mode from 200nm – 400nm wave length range and sharp peak was obtained at 248nm. The spectrum of above drug is represented in figure 2. Calibration curve was constructed by plotting the absorbance against the concentration and regression equation was computed. The results for linearity study were tabulated in table 5.

Analysis of formulation:

Commercial formulation of "Rostinone" (Sanofi Aventis Pharma India) was purchased from a local pharmacy. Twenty tablets of Rostinone brand containing 10mg of TOL were weighed and finely powdered in a mortar. A quantity of powder equivalent to 10 mg of TOL was weighed accurately and dissolved in 25 ml of Methanol and shaken for 15-20 min .Volume were made up to 100 mL in a volumetric flask. The solution was then filtered through whatmann filter paper to get a clear solution. The formulation was estimated in one concentration range by diluting stock solutions to 10 µg/ml of TOL. The method was validated according to ICH guidelines.

Method Validation:

a. Linearity:

The developed method validated as per ICH guidelines. The plot of absorbance against concentration is shown in figure 3. It can be seen that plot is linear over the concentration range of 1-12 µg/mL with correlation coefficient (r2) of 0.9992.

b. Precision:

Intraday and inter-day precision was determined by repeating the assay for the six times on same day and on two different day. The relative standard deviation for replicates of sample solution was less than 2.0% which meet the acceptance criteria for established method. The obtained results are presented in table 2.

c. Accuracy:

To check the accuracy of proposed method, recovery studies were carried out at 80%, 100%, and 120% of test concentration as per ICH guidelines. The data were presented in table 3 and 4.

d. LOD & LOQ:

The LOD and LOQ were separately determined based on the standard deviation of the intercept and the average value of the slop.

3. RESULT AND DISCUSSION

Beer's law is obeyed over the concentration range of 1-12 µg/mL, using regression analysis the linear equation Y=0.0996x-0.0065 with correlation coefficient of R2 = 0.9992. The limit of detection was found to be 0.19µg/mL. The limit of quantification was found to be 0.627µg/mL. The % purity of TOL in "Rostinone" was found to be 99.52 and 100.64. Precision was calculated with intraday and inter-day variation. Recovery study was performed on formulations and %RSD was to be found.

Method was validated in terms of accuracy and precision. The accuracy of the method was proved by performing recovery studies in commercially available formulation. The results were given in table and show the %RSD was less than 1% at each level and values greater than 99% indicate that proposed method is accurate for the analysis of drug and there is no interference from the excipients present in the formulations. The precision of method was checked in terms of intra-day and inter-day where method were repeated on different day and also repeated on different time periods in same day.

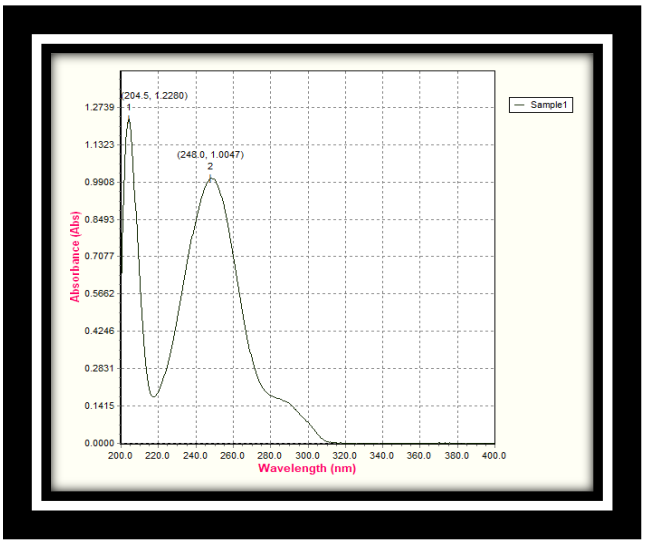

Fig. 2: Spectra of TOL in Methanol

Table No. 1: Optical Parameters for TOL

S. No.	Parameters	Data
1	**λ-Max**	**248nm**
2	**Linearity**	**1-12µg/ml**
3	**Regression equation**	**Y=0.0996X-0.0065**
4	**Correlation coefficient**	**R^2 = 0.9992**
5	**Slop**	**0.0996**
6	**Intercept**	**0.0065**
7	**LOD**	**0.19 µg/mL**
8	**LOQ**	**0.627 µg/mL**

Table No. 2: Precision for Proposed Method

Concentration	Absorbance	Mean	SD	%RSD
Intraday Precision (n = 6)				
10 µg/ml	1.0047	1.00425	0.002324	**0.23146**
	1.0084			
	1.0015			
	1.0029			
	1.0038			
	1.0042			
Inter-day Precision (n = 6)				
10 µg/ml	1.0124	1.01695	0.003034	**0.298373**
	1.0148			
	1.0198			
	1.0162			
	1.0184			
	1.0201			

Table No. 3: Results of Accuracy Study of TOL Bulk drug

Concentration Levels	Concentration (µg/ml)	Mean % Recovery	SD	%RSD
80 %	**8**	99.52	0.885381	**0.891623**
100 %	**10**	100.07	0.602578	**0.597914**
120 %	**12**	**100.64**	**1.008282**	**0.999322**

Table No. 4: Recovery study of TOL Marketed Tablet

Brand Code	Label claim	Level of Recovery (%)	Amount Added (µg/ml)	Recovery (%)
"Rastinone"	**10 mg**	80	8	**100.49**
		100	10	**100.14**
		120	**12**	**100.78**

Table No. 5: Results of Linearity study

S. No.	Concentration Level	Absorbance
1	1.00	0.0865
2	2.00	0.1898
3	4.00	0.4092
4	6.00	0.5882
5	8.00	0.7784
6	10.00	1.0047
7	12.00	1.1812
Correlation Coefficient		**0.9992**

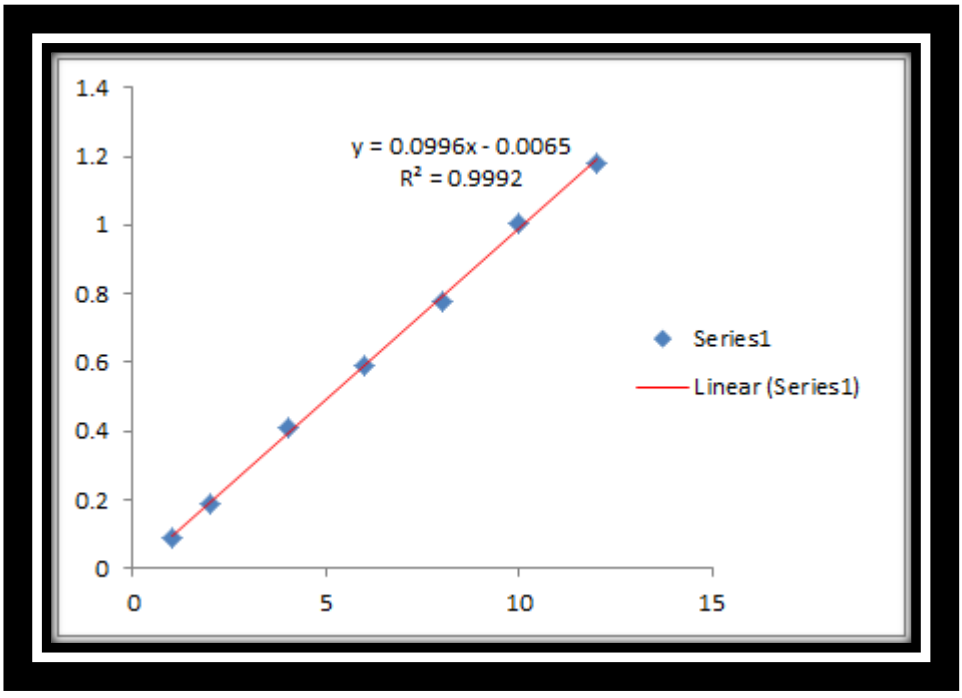

Fig. 3: Correlation coefficient Curve of TOL

Table No. 6: Results of Ruggedness

Parameters	ANALYST – I	ANALYST – II
Mean	100.62	100.11
Standard Deviation	0.53	0.90
% RSD	0.72	0.86

4. CONCLUSION

Simple UV-Spectrophotometric methods have been developed and validated for the determination of TOL in bulk and tablet dosage form. The results of the validation parameters show that the UV spectrophotometric methods were found to be accurate, precise and sensitive. Because of cost-effective and minimal maintenance, the present UV spectrophotometric methods can be preferred at small scale industries and successfully applied and suggested for the quantitative analysis of TOL in pharmaceutical formulations for QC, where economy and time are essential and to assure therapeutic efficacy.

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