International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 4 July-Aug 2022, pp: 160-173 www.ijprajournal.com ISSN: 2456-4494

Development of Uv Spectrophotometric Method For The Estimation Of Sorafenib Tosylate In Bulk And Its Formulation

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Submitted: 01-07-2022 Accepted: 10-07-2022

ABSTRACT

The aim of the present work was to in accurate ,precise reproducible and economical uv spectrophotometric for the estimation of sorafenib tosylate in bulk and its formulations .The uv spectrophotometric was carried out using methanol as solvent. The max absorbance is[λmax] 265 nm was selected for the analysis of sorafenib tosylate respectively. The method was validated according to International Conference on Harmonization guidelines and successfully applied to marketed formulations. The method was founded to be linear in the concentration range of 3-15 mg /ml/with the regression equation on equation y=0.085x

Keywords : sorafenib tosylate , UV spectrophotometry estimation.

I. INTRODUCTION

3-(trifluoromethyl) phenyl] carbamoyl} amino) he chemical name for Sorafenib is 4-[4-({[4-chloro- phenoxy]-N-methyl pyridine-2-carboxamide. Sorafenib is used in the treatment of renal cell carcinoma & colon cancer. From the extensive literature survey reveals that not many UV analytical methods published to describe the quantification of Sorafenib by LC-MS/MS, LC-MS, HPTLC UPLC, HPLC-MS, RP-HPLC, UV-Spectrophotometric method[12]. Infact the published UV method utilizes only methanol as solvent. But there is no stability indicating UV method with acetonitrile and methanol as solvent . These stability indicating methods would be helpful in establishing the stability data of these drugs in bulk and tablet dosage forms.Generally this UV technique is less expensive and with inherent simplicity. Quick development in the pharmaceutical industries, producing more number of new drugs and formulations in different parts of world has been increasing. For getting effective and safe drug formulation to consumers direly needed. So innovative novel analytical methods compulsory for controlling their quality and amount of drug in pharmaceutical dosage forms particularly it plays an vital role in the case of powerful drugs. So the author inclined to select a novel, fast stability indicating UV spectrophotometric analytical method to quantify Sorafenib in bulk and tablet dosage forms. Figure 1 shows the structure of Sorafenib.

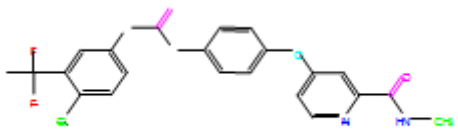

Figure 1: Chemical structure of Sorafenib.

II. METHODOLOGY

Materials and methods :

•ELICO Double beam SL ultra violet –visible spectrophotometer consisting two matched quartz cells with one cm light path
•Electronic balance (key Roy)
•Sorafenib Tosylate Drug sample obtained as a gift sample
•Distilled water.
•Methanol.
•Sorafenib Tosylate 200 mg tablets (Nexavar)

Determination of solubility

The sample is dissolved in various solvents and tested for solubility .

It is very slightly soluble in ethanol and water sorafenib tosylate was found to be soluble in

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methanol . Its solubility in methanol is 10 mg/ml So methonal was selected as solvent.
Selection of detection wavelength To determine the optimum λ max, sorafenib tosylate 10 µg /ml of working standard solution was prepared and scanned in UV wavelength range of 200-400 nm utilizing methanol as blank. It was observed that the drug showed maximum absorbance at 265 nm as represented in fig:1

Determination of stability

sample solution (10µg/ml) was taken for determining the stability of the drug in the selected solvent absorbance was measured every 15 minutes for three hours given in table :1

Preparation of stock solution and working standard solutions

Sorafenib tosylate 100µg/ml standard stock solution was prepared by transferring precisely weighed 10 mg of standard sorafenib tosylate into 100ml volumetric flask and dissolved in a few ml of methanol. The solution is sonicated for 15 minutes and the solution was made up to 100ml by using methanol and thus a solution of 100µg /ml concentration was obtained.

Preparation of calibration curve

A calibration curve was plotted over a concentration range of 3-15µg/ml for sorafenib tosylate by taking sorafenib tosylate stock solution 0.3,0.6,0.9,1.2,1.5 ml was shifted to a series of 10ml volumetric flask and make up the volume with methanol up to the mark. calibration curve was prepared by taking readings at lambda max 265nm and plotted a graph by taking sorafenib tosylate concentration on X-axis and their respective absorbance on Y-axis . calibration data is shown in figure 3.

Formulation linearity

10 tablets of sorafenib tosylate 200 mg were weighed accurately and powdered by using mortar and pestle. The powder equivalent to 10mg of drug is taken into100ml volumetric flask and dissolved in a few ml of methanol .The solution is sonicated for 15 min and solution was made up to 100ml by using methanol and then solution filtered thus solution of 100µg/ml concentration was obtained from the filtrate pipette out 0.3,0.6,0.9,1.2,1.5ml into a series of 10ml volumetric flask and make up the volume with methanol giving solution concentration 3,6,9,12,15 µg/ml were prepared .The absorbance values of these were measured at 265 nm .

Accuracy

To check the accuracy of the developed method and to study the interference of formulation excipients, analytical recovery studies were carried out by taking 6µg/ml solution of formulation in each of three 10ml volumetric flask and then adding 3,6,9µg / ml of raw material the solutions were prepared in triplicate and the accuracy was indicated by percentage recovery.

Precision

To check the precision of the proposed method the recovery studies performed three times in same day (intra –day) and recovery studies between days (inter –day) were analysed . the realative standard deviation of intra –day and inter –day values were calculated and given in table – 4,5,6,7,8,9The precision is expressed in the form of percent relative standard deviation `.

Limit od detection and limit of quantification

Six linearity were performed by using standard sorfenibtosylate and slope values for each linearity were calculates.
The limit of detection and limit of quantification were calculated based on the standard deviation slope of calibration curve .
The following formulae were used to calculate the LOD and LOQ values .
LOD =3.3σ/S
LOQ=10σ/S
Where, σ =standard deviation of the responses S= slope of the calibration curve.

III. RESULTS AND DISCUSSIONS

Determination of λmax

For the selected drug sample, maximum absorbance was determined .It was found to be 265nm and it is represented in fig .1

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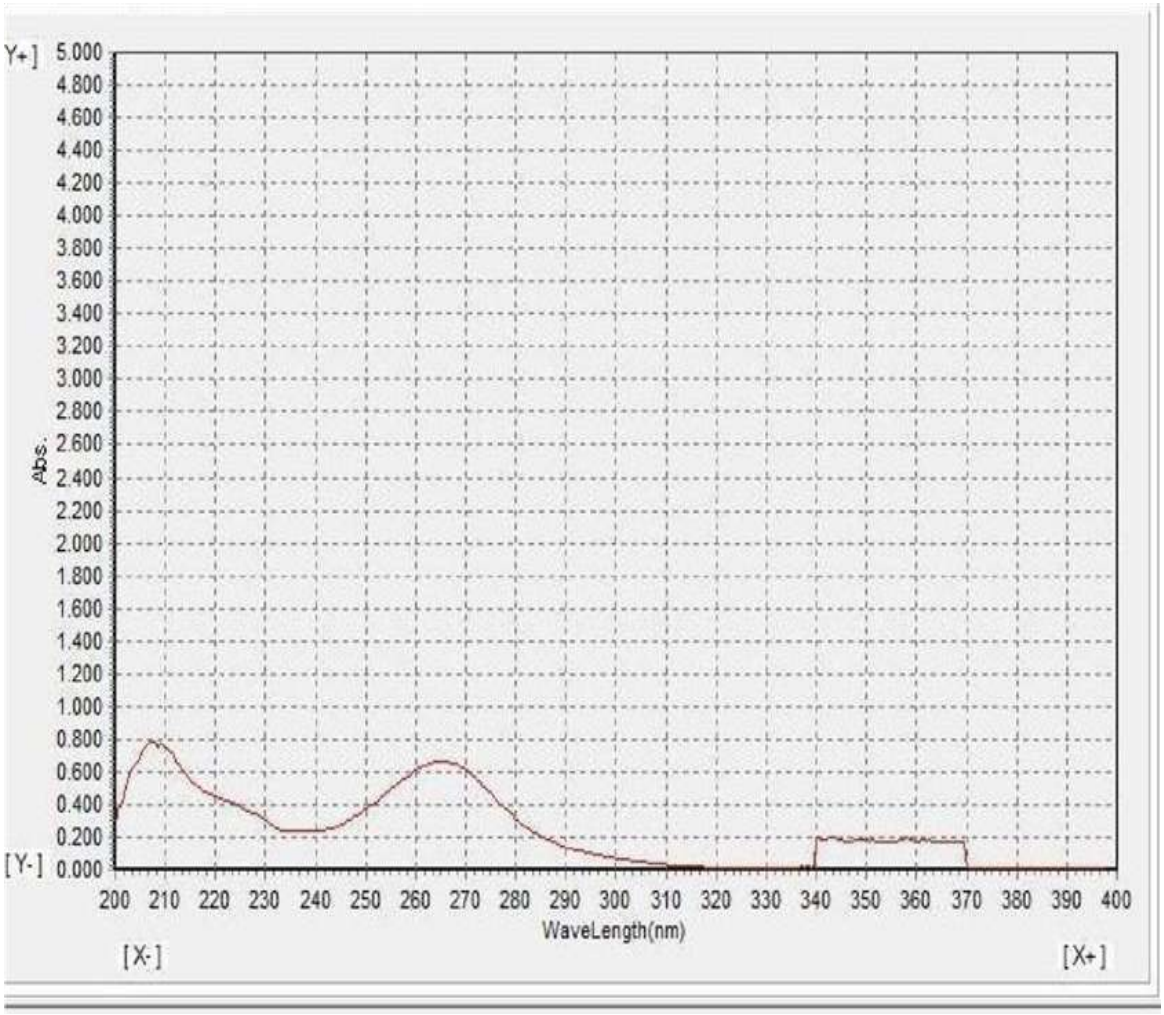

Fig 2 : Absorption spectrum of sorafenib Tosylate

Determination of stability

The absorbance of 10 µg/ml of sorafenib tosylate was measured every 15 minutes for 3 hours the values are consistent throughout the experiment as can be seen in table 1

S. No	Time	Absorbance (AU)
1	0	0.67
2	15	0.697
3	30	0.696
4	45	0.697
5	60	0.696
6	75	0.696

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7	90	0.695
8	105	0.694
9	120	0.696
10	135	0.695
11	150	0.696
12	165	0.695
13	180	0.695

Table: 1 stability study

Preparation of calibration curve

From the absorbance values a calibration curve was plotted in the desired concentration range. the curve obtained was linear with correlation coefficient 0.999which represented in fig 3

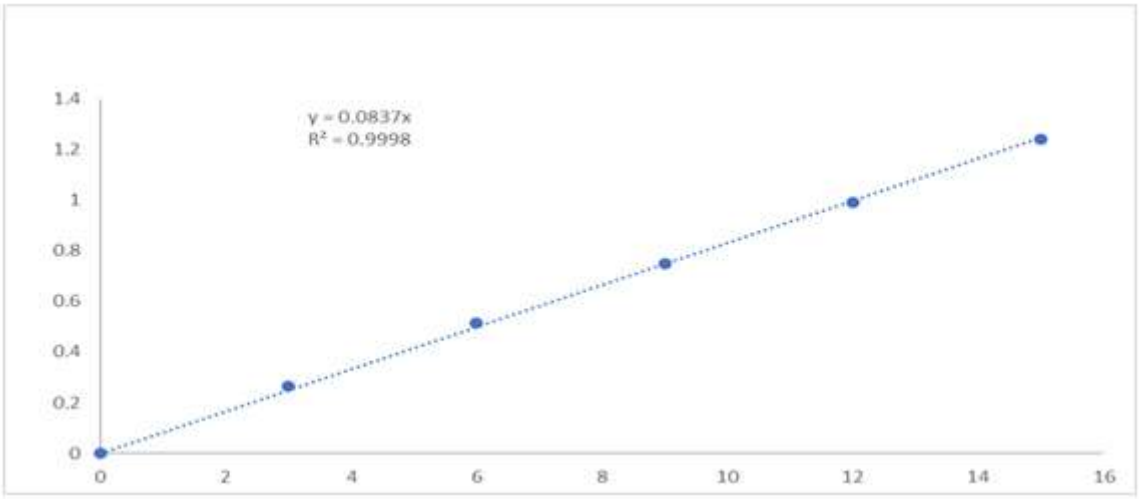

Fig 3 calibration curve of sorafenib tosylate

LOD and LOQ

The limit of detection and limit of quantification were determined by taking 6 linearity and average slope. these were represented in figure 4,5,6,7,8,9

The values of LOD and LOQ for the proposed method were found to be 0.0304µg/ml and 0.0921µg/ml respectively and are represented in the table 2

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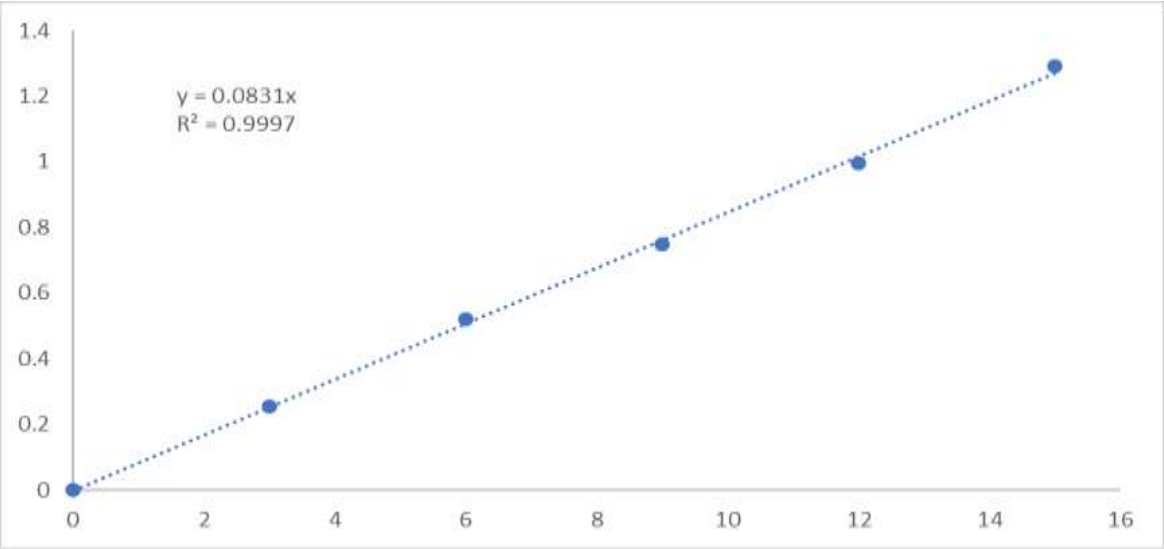

Fig 4(linearity curve 1)

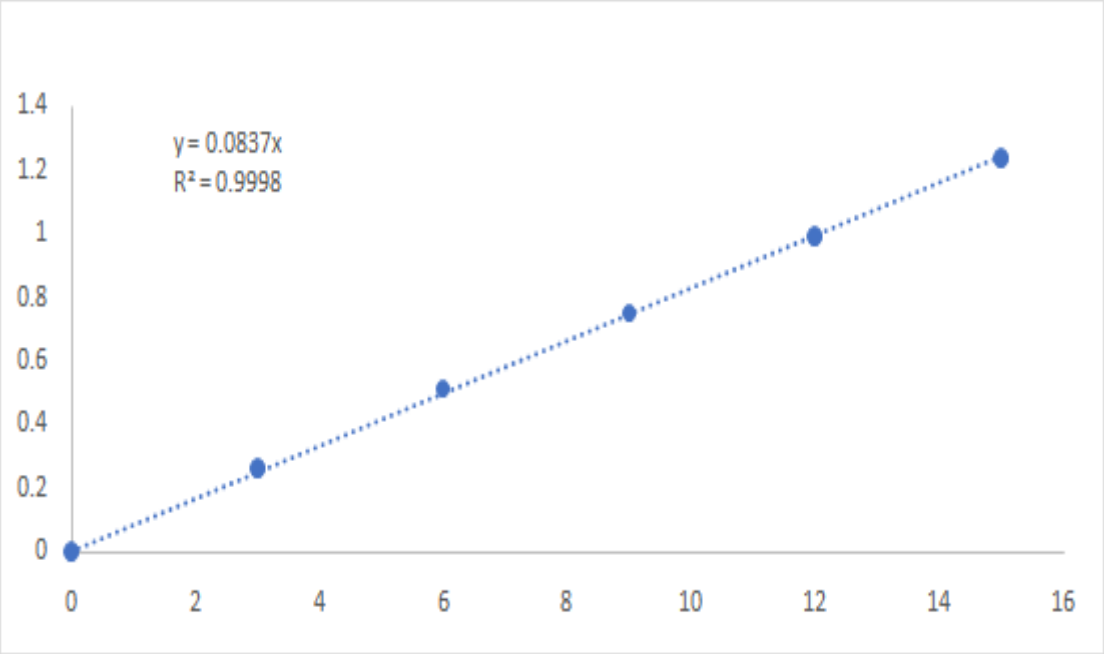

Fig 5 (linearity curve 2)

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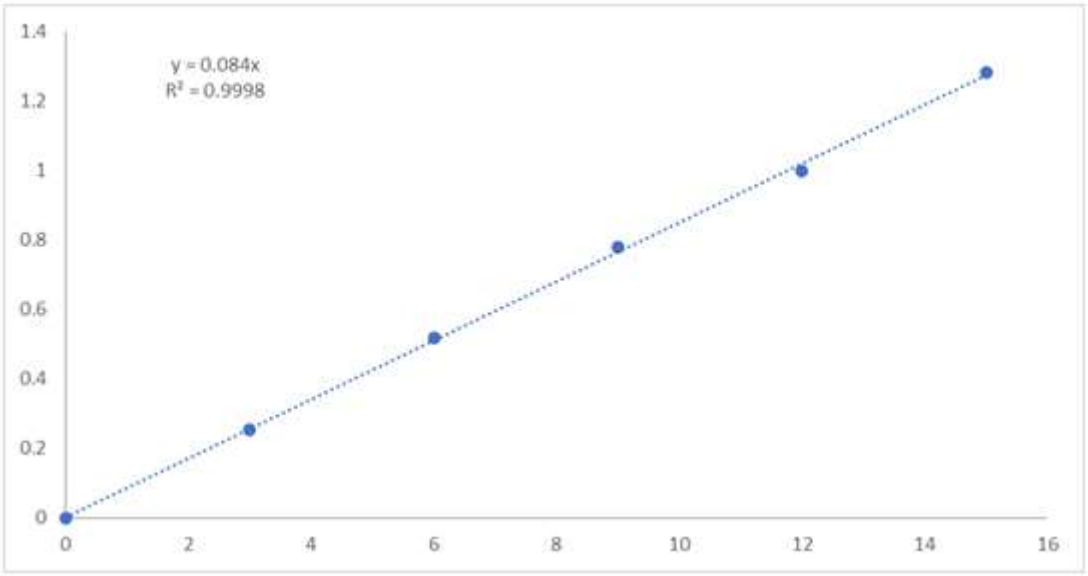

Fig 6:(linearity curve 3)

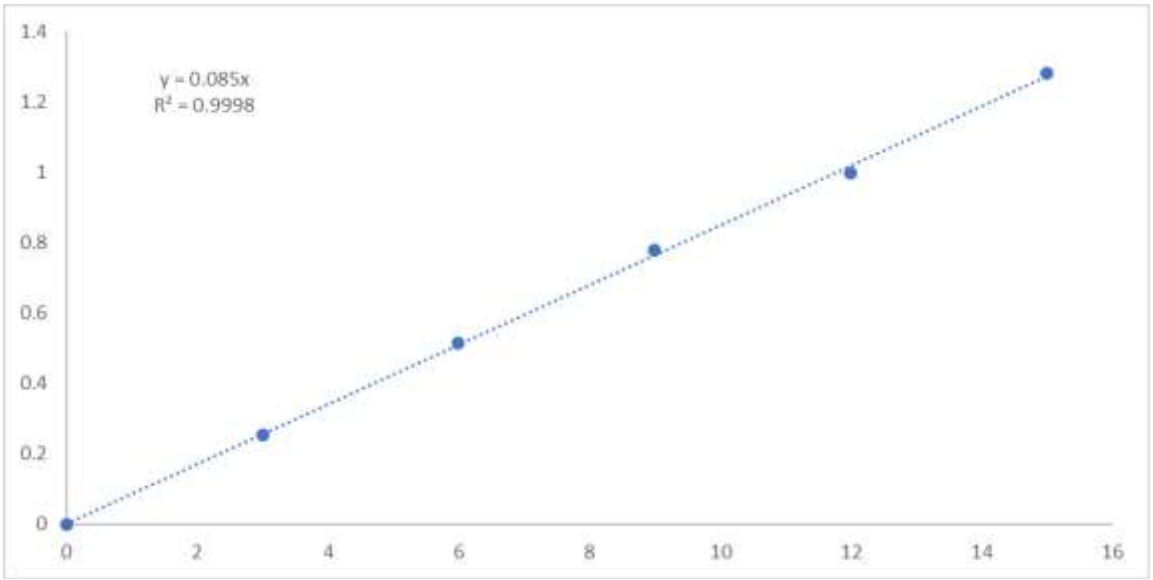

Fig 7 :(linearity curve 4)

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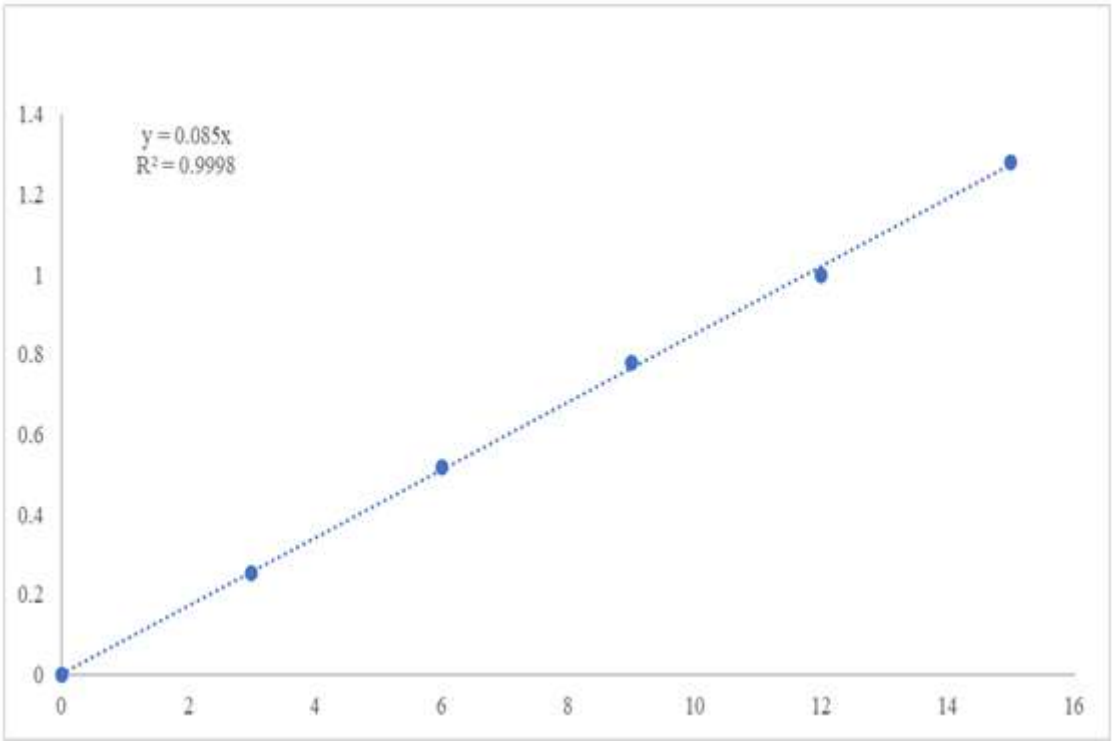

Fig 8 :(linearity curve 5)

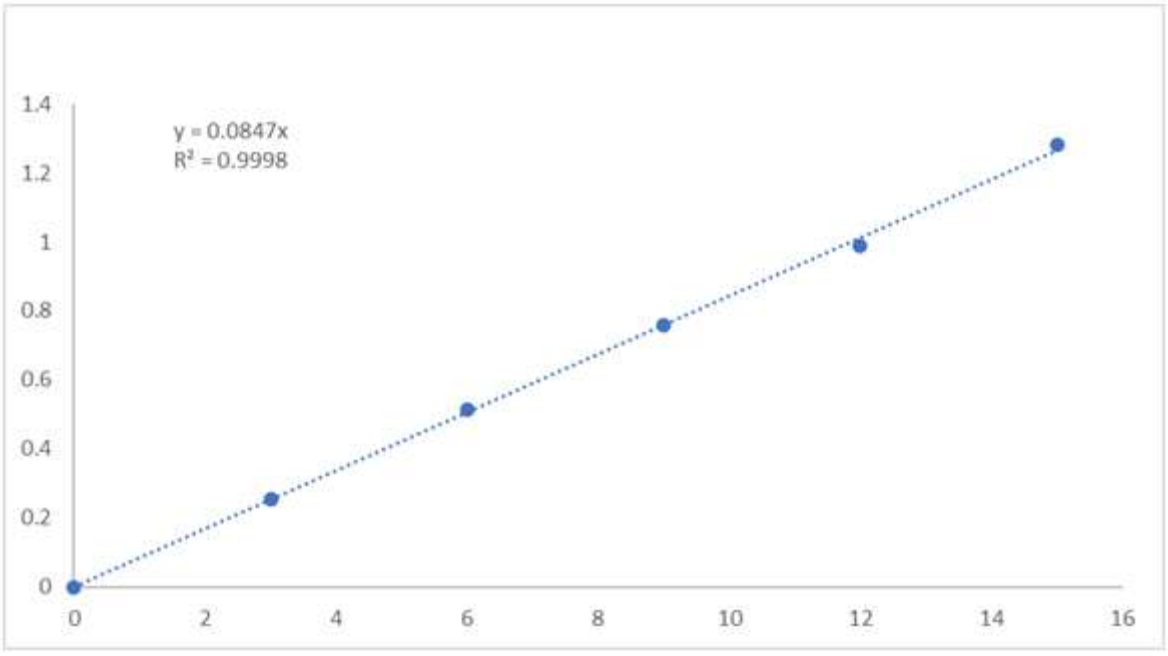

Fig 9: (linearity curve 6)

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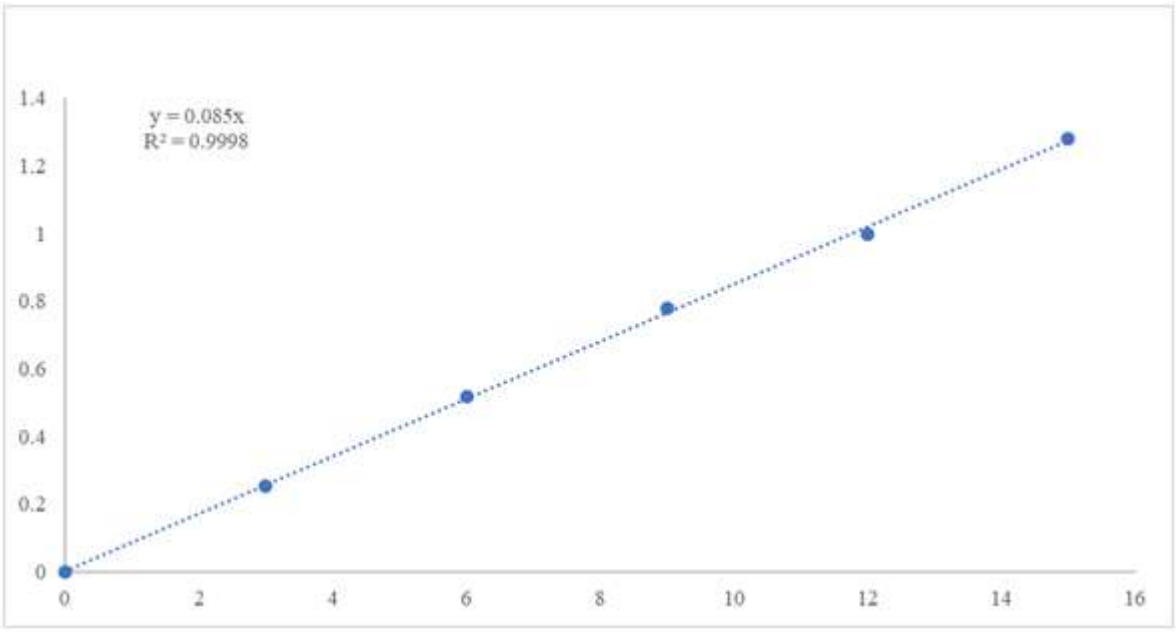

Fig 10 Formulation of linearity curve

S. No	Slope	LOD (µg/ml)	LOQ(µg/ml)	SD
1	0.0837	0.0304	0.0921	0.00077
2	0.0831			
3	0.0847			
4	0.0844			
5	0.85			
6	0.854			

Table 2 :LOD and LOQ

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Accuracy

The accuracy of the method was proved by performing recovery studies for commercially available formulations of sorafenib tosylate. the standard deviation value is 1.0453 and %recovery value is 1.0387 recovery of sorafenib tosylate in formulations was found to be with in the accepted limits and is represented in table :3

Precision

It was found that the %RSD values of intra –day and inter -day precision were 1.1436 and 0.92066 . Respectively pertaining to sorafenib tosylate and the values of RSD% [<2.0] clearly show that the method is fairly precise is represented in table 4,5,6,7,8,9

S. No	Amount of Drug present (µg/ml)	Amount Added (µg/ml)	Amount Recovered (µg/ml)	Percentage	SD	RSD
1	6	3	3.01	100.33	1.0453	1.0387
2	6	3	3.04	101.33		
3	6	3	3.10	103.33		
4	6	6	5.99	99.88		
5	6	6	6.011	100.18		
6	6	6	6.001	100.01		
7	6	9	9.02	100.22		
8	6	9	9.05	100.55		
9	6	9	8.11	99.88		

Table 3 Recovery study of sorafenib tosylate

S. No	Amount of Drug present (µg/ml)	Amount Added (µg/ml)	Amount Recovered (µg/ml)	Percentage	SD	RSD
1	6	3	3.01	100.33		
2	6	3	3.04	101.33		

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3	6	3	3.10	103.33	1.0453	1.0387
4	6	6	5.99	99.88		
5	6	6	6.011	100.18		
6	6	6	6.001	100.01		
7	6	9	9.02	100.22		
8	6	9	9.05	100.55		
9	6	9	8.11	99.88		

Table 4 (Intra- day recovery -1)

S. No	Amount of Drug present (µg/ml)	Amount Added (µg/ml)	Amount Recovered (µg/ml)	Percentage	SD	RSD
1	6	3	3.06	102.00	0.9182	0.9146
2	6	3	3.04	101.33		
3	6	3	3.05	101.66		
4	6	6	5.98	99.66		
5	6	6	5.97	99.05		
6	6	6	5.98	99.66		
7	6	9	8.99	99.88		
8	6	9	8.992	99.81		
9	6	9	9.00	100.00		

Table 5 (Intra- day recovery -2)

S. No	Amount of Drug present (µg/ ml)	Amount Added (µg/ ml)	Amount Recovered (µg/ml)	Percentage	SD	RSD
1	6	3	3.12	104.00		
2	6	3	3.10	103.33		

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3	6	3	3.09	103.00	1.5005	1.4776
4	6	6	5.98	99.66		
5	6	6	6.01	100.16		
6	6	6	6.03	100.5		
7	6	9	9.02	100.22		
8	6	9	9.09	101.00		
9	6	9	9.10	102.11		

Table 6: (Intra- day recovery -3)

S. No	Amount of Drug present (µg/ml)	Amount Added (µg/ml)	Amount Recovered (µg/ml)	Percentage	SD	RSD
1	6	3	3.02	100.66	0.3207	0.31840
2	6	3	3.01	100.33		
3	6	3	3.04	101.33		
4	6	6	6.09	100.16		
5	6	6	6.03	100.05		
6	6	6	6.02	100.33		
7	6	9	9.10	101.11		
8	6	9	9.08	100.88		
9	6	9	9.12	101.33		

Table :7 (Inter day recovery -1)

S.No	Amount of Drug present (µg/ml)	Amount Added (µg/ml	Amount Recovered (µg/ml)	Percentage	SD	RSD
1	6	3	3.12	104.00	1.4876	1.4601
2	6	3	3.10	103.33		
3	6	3	3.12	104.00		

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4	6	6	5.98	99.66		
5	6	6	6.01	100.16		
6	6	6	6.07	101.16		
7	6	9	9.12	101.33		
8	6	9	9.16	101.77		
9	6	9	9.14	101.33		

Table :8 (Inter day recovery -2)

S.No		Amount of Drug present (µg/ml)	Amount Added (µg/ml)	Amount Recovered (µg/ml)	Percentage	SD	RSD
	1	6	3	3.06	102.00	1.0135	1.0004
	2	6	3	3.07	102.33		
	3	6	3	3.10	103.33		
	4	6	6	6.00	100.00		
	5	6	6	6.04	100.66		
	6	6	6	6.02	100.33		
	7	6	9	9.10	101.11		
	8	6	9	9.08	100.88		
	9	6	9	9.10	101.11		

Table :9 (Inter day recovery -3)

IV. SUMMARY & CONCLUSION

SUMMARY

A UV spectrophotometric method has been developed and validated for determination of sorafenib tosylate in its pure form and its pharmaceutical dosage forms.

The process was done by using methanol as a solvent with the detection wavelength set at 265nm. Sorafenib tosylate was checked for its stability in the chosen solvent and found to be stable. the method was linear with correlation coefficient 0.999 in the concentration range of 3-15µg/ml. the limit detection and limit quantification were 0.0304µg/ml and 0.0921µg/ml respectively. the intra and inter -day precisions were satisfactory; the relative standard deviations did not exceed 2%.the accuracy of the method is high as can be seen from the mean recovery values of sorafenib tosylate which were in the range of 99.12-99.85%.the method met the ICH regulatory requirements. the results of validation are summarized in table 10

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S.NO	Parameter	Results
1	Detection of wavelength	265λmax
2	Beer-Lambert law (µg/ml)	3-15(µg/ml)
3	Regression equation (y=mx+c)	Y=0.0837
4	Correlation (r^2)	0.9998
5	Accuracy (%mean recovery)	100.63
6	LOD	0.0304 µg/ml
7	LOQ	0.0921 µg/ml
8	Intra -day (%RSD)	1.1436
9	Inter-day (%RSD)	0.9263

Table :10 the results of validation are summarized

Conclusion:

A simple, economical, rapid, precise and accurate UV spectrophotometric method was developed for the estimation of sorafenib tosylate in bulk and pharmaceutical formulations The method was developed by using methanol as solvent .the developed method was validated for parameters viz accuracy ,precision ,linearity ,limit of detection and limit of quantification as per ICH guide lines .All the parameter were found to be within the acceptance limits . the results indicated that the proposed method for estimation of sorafenib tosylate is very accurate and cost effective and can be employed in routine sample analysis of sorafenib tosylate in bulk and pharmaceutical formulation.

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