ISSN: 0974-2115
www.jchps.com Journal of Chemical and Pharmaceutical Sciences

VALIDATED UV SPECTROPHOTOMETRIC METHOD FOR QUANTITATIVE ANALYSIS OF CAPECITABINE IN PHARMACEUTICAL DOSAGE FORM

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ABSTRACT

Rapid, simple and sensitive spectrophotometric methods are presented for the determination of Capecitabine. The methods are based on their oxidation and precipitation reactions. In this method the reactions can be monitored spectrophotometrically by measuring the absorbance of the Capecitabine at 245nm. The proposed methods have permitted the quantification of Capecitabine over linearity in the range of 2-10 µg/ml and its percentage recovery was found to be 99.451 to 101.166.

KEY WORDS: Capecitabine, Spectrophotometric methods, Statistical analysis, Recovery studies.

1. INTRODUCTION

Capecitabine (CAP) is an orally administered chemotherapeutic agent used in the treatment of colorectal cancer, metastatic breast cancer, stomach, pancreas, liver, esophageal and skin cancers. It is chemically pentyl[1-(3,4-dihydroxy-5-methyl tetrahydrofuran-2-yl)-5-fluoro-2-oxo-1H-pyrimidin-4-yl]carbamate (Fig.1). Oral CAP is a prodrug which undergoes sequential hydrolysis and deamination reactions in the liver to produce 5'-deoxy-5-fluorouridine. This is converted to 5-fluorouracil (5-FU) by thymidine phosphorylase (also known as platelet-derived growth factor). As this enzyme is abundant in tumor tissue there is some tumor specificity in the patient's exposure to 5-FU. 5-FU in turn inhibits the thymidylatesynthetase, blocking the methylation of deoxyuridylic acid to thymidylic acid, interfering with DNA, and to a lesser degree, RNA synthesis and decreases growth of tumor tissue. Since it lacks selectivity towards tumor cells, 5-FU also exhibits significant toxicity. Prodrugs of 5-FU like CAP have been developed to improve efficacy and to reduce side effect toxicity.

2. MATERIALS AND METHODS

UV-Visible Spectrophotometer (Systronics model 2203). The UV-VIS spectrophotometer achieves a resolution of 1 nm with matched quartz cells of 1 cm path length.CAP working standard manufactured by Hetero Drugs Ltd., Hyderabad, Andhra Pradesh, India. Analytical grade Methanol, Distilled waterand CAPIIBINETablets containing 500 mg of CAP are manufactured by Dr.Reddy's Laboratories Pvt. Ltd., Hyderabad, India.

Preparation of standard drug solutions:10mg of CAPpure drug was accurately weighed, transferred into a 100ml volumetric flask containing 50 ml ofmethanol and sonicated for about 10 minutes. The volume was made up to the mark with distilled waterto get the stock solution (100µg/ml). This solution was further diluted with the same to get the working standard solution.

Preparation of Calibration curve: Aliquots of standard drug (0.2 ml to 1.0 ml, 100µg/ml) solution in methanol and distilled water (50:50%v/v) were transferred into a series of 10 ml volumetric flasks and the solution was made up to 10ml with methanol and water (50:50%v/v). After setting the instrument for its spectral properties the solutions were scanned in the wavelength ranging from 190nm-400nm. The wavelength of maximum absorption for CAPwas found at 245nm. Calibration curve was prepared by plotting concentration of CAP on x-axis and their respective absorbances on y-axis.

Procedure for assay of pharmaceutical formulations: Ten tablets of CAP marketed formulationwere weighed and powdered. A quantity of tablet powder equivalent to 50mg of CAP was accurately weighed and transferred into a 100ml volumetric flask containing 50 ml of methanol and distilled water (50:50%v/v). The solution was sonicated for extracting the drug for about 15minutes, filtered through a cotton wool and the filtrate was made up to volume with methanol and distilled water (50:50%v/v). Transfer 0.1ml of the filtered sample solution to 10ml volumetric flask and made up to volume with distilled water. The absorbance of the resulting solution was measured at 245 nm and the amount of CAPwas computed from its calibration plot.

Validation of the developed method:

Precision: Precision was determined by intra-day and inter-day study. Precision of the method was evaluated by carrying out the assay and analyzing corresponding responses 6 times on the same day and on different days for the sample solution. The percent relative standard deviation (% RSD) was calculated.

Accuracy (Recovery studies): Accuracy studies were performed at three different levels (80%, 100% and 120%) and the samples were analyzed in triplicate by the proposed method. Known amount of standard CAP at 80%, 100% and 120% of predetermined sample was added to a pre quantified tablet sample.

LOD and LOQ: Limit of Detection and Limit of Quantitation were calculated using following formula LOD= 3.3(SD)/S and LOQ= 10 (SD)/S, where SD=standard deviation of response (absorbance) and S= slope of the calibration.

3. RESULTS AND DISCUSSION

The proposed method obeyed Beer's law in the concentration range of 2-10 µg/ml. The optical characteristics and the data concerning to the proposed method is represented in Table 1. The limit of detection and limit of quantitation for estimation of CAP were 0.29987µg/mL, 0.90871µg/mL respectively. Precision study was performed and represented in Table 2. Recovery studies were carried out for the developed method by addition of known amount of standard drug solution of CAP to pre-analyzed tablet sample solution at three different concentration levels. The resulting solutions were analyzed by the proposed methods. The recovery (Table 3) was in the range of 99.451 to 101.166 percentages. The assay results were tabulated in Table 4.

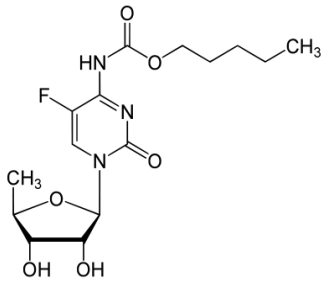

Figure.1.Chemical structure of Capecitabine

Table.1.Optical characteristics, regression data of the proposed method

Parameter	Result
λ_{max} (nm)	245
Beer'slawlimits(µg/ml)	2-10
Molarabsorptivity (L. $mole^{-1}$ cm^{-1})	$1.716x10^4$
Detectionlimits (µg/ml)	0.299874
Quantitationlimits (µg/ml)	0.908710
Sandell's sensitivity (µg/cm^2/0.001absorbanceunit)	0.020920
Regression equation(Y=a+bc): Slope(b)	0.0481
Standarddeviationof slope(S_b)	0.000522
Intercept(a)	-0.0032
Standarddeviationofintercept(S_a)	0.003163
Standarderrorofestimation(S_e)	0.004371
Correlationcoefficient(r)	0.9997
%Relativestandarddeviation*	1.423

***Average of six determinations.**

Table.2.Results of precision study

Precision*	Intra-day	Inter-day
Mean % recovery	99.667	99.736
SD	0.939	1.224
%RSD	0.942	1.227

***average of six determinations**

Table.3.Results of accuracy study

Accuracy*	Mean % recovery ± SD	%RSD
80%	100.685 ± 0.480	0.477
100%	100.042± 0.953	0.952
120%	99.829 ± 0.378	0.378

***average of three determinations**

Table.4.Assay results

Formulation	Labeled amount	Amount found	Mean % recovery ± SD	% RSD
CAPIIBINETablets **(**Dr.Reddy's Laboratories Pvt. Ltd., Hyderabad**)**	500 mg	495.218	99.547 ±1.417	1.423

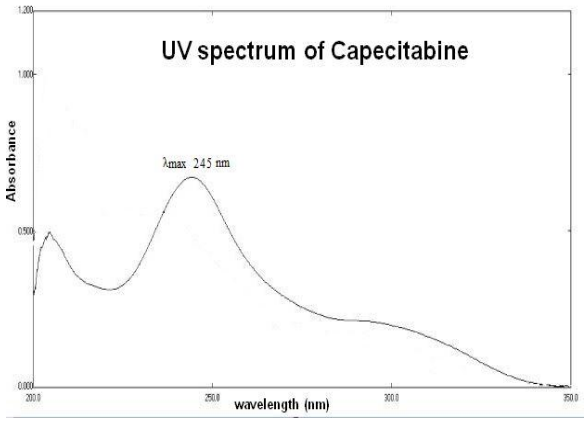

Figure.2.UV spectrum of Capecitabine

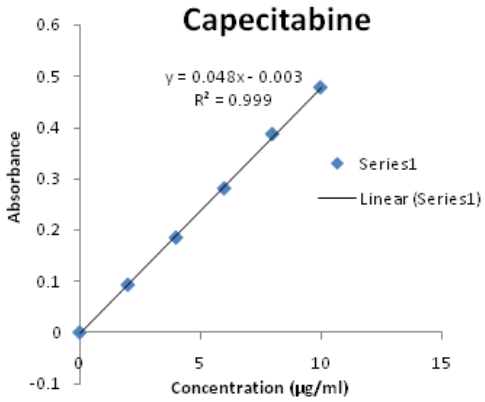

Figure.3.Calibration curve of CAP by UV method

4. CONCLUSION

The present study demonstrated an UV spectrophotometric method for the estimation of CAPavailable as tablet dosage form. From the above experimental data results and parameters, the developed method has advantages like the time taken for preparation of standard and sample solutions is less and hence suitable for the analysis ofCAP raw material and its pharmaceutical dosage form. Infact the method developed for CAP was found to be simple, precise, accurate and cost effective and it can be effectively applied for routine analysis.

5. ACKNWOLEDGEMENTS

The authors would like to thank Hetero Labs for providing the samples of CAP. We are highly grateful to Dr.L.Rathaiah, Honorable Chairman, Vignan group of institutions, Vadlamudi, Guntur, for providing the necessary facilities to carry out this research work.

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