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Development and Validation of A Simple and Specific UV Spectrophotometric Method for Capecitabine Assay in Active Pharmaceutical Ingredients (API) and in its Dosage Forms

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G. Ramesh[1] and M. Subba Rao*

*[1,]*Department of Chemistry, Acharya Nagarjuna University, Guntur, Andhra Pradesh, India*

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ABSTRACT

A rapid, simple, accurate, and economical UV-spectrophotometric method has been developed and validated for the assay of the anti-neoplastic agent capecitabine in active pharmaceutical ingredients (API) and in its dosage forms. The analysis of capecitabine is based on the UV absorbance maxima at about 243.60 nm wavelength, using methanol as solvent. Similarly, a sample of ground tablets were extracted with methanol, centrifuged, and diluted with the same solvent. The absorbance of the sample preparation was measured at 243.60 nm against the solvent blank, and the assay was determined by comparing with the absorbance of a similarly prepared 10µg/mL standard solution of capecitabine. The calibration graph was linear from 2.5µg/mL to 15µg/mL for capecitabine with the correlation coefficient being more than 0.9999. The relative standard deviation of the replicate determination for precision was about 0.71%. The percent recovery of accuracy was within the range of 99.93%–101.22%, indicating insignificant interference from the other ingredients in the formulations. The proposed UV-spectrophotometric method can be applied as alternative method for the routine QC quantitation of capecitabine in API and in dosage forms.

INTRODUCTION

Capecitabine [**Figure.1**] [1-4], Pentyl [1-(3, 4-dihydroxy-5-methyl-tetrahydrofuran-2-yl)-5-fluoro-2-oxo-1H-pyrimidin-4-yl] aminomethanoate is a fluoropyrimidine carbamate chemotherapeutic agent orally-administered used in the treatment of metastatic breast and colorectal cancers. It is used in combination with other medications to treat breast cancer that has come back after treatment with other medications. Few analytical methods [5-13] for quantitative determination of capecitabine were reported in the literature and these methods were applied for the determination of capecitabine and its metabolites in biological fluids. The main objective of present work was to develop simple, sensitive specific spectrophotometric method for detection of capecitabine in bulk as well as dosage forms.

EXPERIMENTAL

Instrumentation

Shimadzu UV/Vis Spectrophotometer (Model-2450) equipped with UV probe software was used in the present assay. For dilutions various micropipettes of volumes 10-100µL was used. All weighing operations were done on Shimadzu Digital Analytical Balance (Japan) and standard glass ware (Borosil Make) was used for preparing of solution.

Chemicals and Reagents

Capecitabine (99.9% Pure) used was supplied by Dr Reddys Labs. Hyderabad and formulation of capecitabine in the brand name of Xeloda (strength: 500mg Capecitabine) from Nicholas Piramal India Ltd were purchased from local pharmacy. Methanol of analytical grade was purchased from local vendor and was used for the preparation of standard and sample solutions without further purification.

Diluent

Methanol of analytical grade was used as diluent in the present assay. It is used as received.

Standard Preparation

Accurately weighed 100 mg of capecitabine test standard was transferred to a 100 mL volumetric flask containing 25 mL of methanol solvent. This was sonicated for about 5 min to dissolve it and the resultant solution was diluted to 100 mL with methanol solvent (Diluent). Working

standard solutions in concentration range of 2.5 -15µg/mL were prepared by transferring aliquot of the above stock solution with micropipette to a series of different 100 mL and diluted to the mark with the same diluent.

Preparation of Sample Solution

10 Tablets of dosage form (Xeloda**;** strength: 500mg) of capecitabine was weighed and powdered in glass mortar. The powder equivalent to 100mg was transferred into a 100mL clean dry volumetric flask, 70mL of diluent was added to it and was shaken by mechanical stirrer and sonicated for about 30 minutes by shaking at intervals of five minutes each and was diluted up to the mark with diluent and allowed to stand until the residue settles before taking an aliquot of this solution was further diluted into a series of 10mLvolumetric flask and diluted with diluent up to the mark, filtered through 0.45µm filter to obtain concentration that obey in beers law limit.

RESULTS AND DISCUSSION

ANALYTICAL METHOD DEVELOPMENT

a. Determination of λ_{MAX}:

Working standard solution of 10µg/mL of capecitabine prepared was subjected to scanning between 200 – 400 nm and the absorption maximum was determined and an optimal response was obtained at 243.60 nm. This wavelength of 243.60nm was used for the quantification of standard and in dosage forms of capecitabine respectively. The absorption spectrum so obtained was shown in **Figure.2**.

b. Procedure

After preparation of standard and tablet solutions, the absorbances of the sample preparation and standard preparation were measured at this fixed wavelength (λ**max** 243.60 nm) and the quantity of capecitabine in standard and in dosage forms was calculated.

METHOD VALIDATION

The developed UV spectrophotometric method is validated as per ICH norms.

a. Specificity

The absorbance values of Standard and Sample are identical with nearly same values exhibiting good specificity.

b. Linearity

The linearity of the proposed method was established by determining the absorbance of different working concentrations of capecitabine drug substance in triplicate over a range of 25% (2.5µg/mL) to 150% (15.0µg/mL) of the normal sample preparation. The calibration curve was graphed, as plot of absorbance vs concentration in µg/mL of capecitabine, and was found to be linear with correlation coefficient more than 0.999 [Table.1 & Figure.3] indicating the linearity of the proposed method with optimum value of standard error for the entire analytical medium used.

c. LOD and LOQ

The detection and quantization limits were found to be 0.177 and 0.592 for capecitabine.

d. Precision

The precision of the present proposed method was performed in six replicates of fixed concentration of capecitabine and the percentage relative standard deviation (%RSD) was measured. The %RSD of 0.71 tabulated ((Table.2) was found to be not more than 2.0% revealing good precision of the proposed method.

e. Accuracy

The accuracy of the method was established by adding the capecitabine test standard solution of the pre-analyzed tablet formulation. The analysis at each level was performed in triplicate and the mean recovery of capecitabine was measured (Table.3). The percent recovery at each level was found to be well within the range of 99.93% - 101.22%, indicating insignificant interference from the excipients.

f. Ruggedness

The ruggedness of the method of capecitabine was established by having the precision study performed on another instrument by another analyst. The cumulative %RSD for content of capecitabine for the samples of ruggedness study were found to be not more than 2.0 % (Table.4).

g. Solution stability

The absorbance of the same sample solution of capecitabine at the initial stage and intervals of 4 hours, 8 hours, 12 hours, and 24 hours were measured and the cumulative %RSD determined. The %RSD was found to be not more than 2.0%.

h. Assay of dosage forms

Pharmaceutical assay was carried out on available brand of capecitabine (Xeloda; strength: 500mg) from local pharmacy using the developed method and the % assay was calculated and the results were tabulated (Table.5) revealing that the proposed method can be used for routine QC quality control analysis in the API, and tablet formulation.

CONCLUSION

The proposed UV-spectrophotometric method enabled the quantitative determination of capecitabine in bulk drug samples and dosage forms. The calibration curve was linear over a concentration range from 2.5-120µg/mL for capecitabine. The relative standard deviation (R.S.D.) was less than 2.0% and average recovery was around 99.99%. The simplicity and cost effectiveness of the present developed UV-spectrophotometric method can be used as a choice of new alternative analytical method to validate label claims of manufacturers by regulatory authorities.

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REFERENCES

1. Wagstaff AJ, Ibbotson T, Goa KL: Capecitabine: a review of its pharmacology and therapeutic efficacy in the management of advanced breast cancer. Drugs, 63(2),2003,217-36.
2. Walko CM, Lindley C: Capecitabine: a review. Clin Ther, 27(1),2005,23-44.
3. Twelves C: Vision of the future: capecitabine. Oncologist,6(4),2006,35-9.
4. Koukourakis GV, Kouloulias V, Koukourakis MJ, Zacharias GA, Zabatis H, Kouvaris J: Efficacy of the oral fluorouracil pro-drug capecitabine in cancer treatment: a review. Molecules,13(8),2008,1897-922.
5. Kishore M, Jayaprakash M, Vijayabhaskara Reddy T, Spectrophotometric determination of Capecitabine in pharmaceutical formulations,3(1),2011,63-69.
6. Ranjitha Kandimulla, Nagavalli D,Validated estimation of Capecitabine by UV-Spectroscopy, International Research Journal of Pharmacy,3(11),2012,163-166.
7. Sankpal P, Doijad R, Suryawanshi G, Patil P, Pathan A, Simple quantitative method development and validation of Capecitabine in pure form and pharmaceutical dosage form by UV-Spectroscopy. Inventi Rapid: Pharm Analysis & Quality Assurance, 7(11), 2012 26.
8. SreenivasaRao T, Sukanya K, ChandanamSreedhar, Akkamma Hg, Sai Kumar S, Manogna Development and validation of new analytical methods for the estimation of Capecitabine in pharmaceutical dosage form research journal of pharmaceutical, biological and chemical sciences, 3(3), 2012, 713 – 721.

9. Subhashini E, Syama Sundhar B, A novel RP-HPLC method for the determination of capecitabine in pharmaceutical drug products, Research Desk, 1(1),2012,10-17.
10. Ravisankar P, Devala Rao G, Naveen Kumar M, Krishna Chaitanya M, An improved RP-HPLC method for the quantitative determination of Capecitabine in bulk and pharmaceutical tablet dosage form, Der Pharmacia Lettre, 5(3), 2013, 249-260.
11. Narendra Devanaboyina, Development and validation of new RP HPLC method for analysis of capecitabine in pharmaceutical dosage form, IJSIT ,2(1), 2013, 21-30
12. Naveen Kumar M, Ravi Sankar P, Viswanath A, Srinivasa Babu P, Validated UV spectrophotometric method for quantitative analysis of capecitabine in pharmaceutical dosage form, Journal of Chemical and Pharmaceutical Sciences,6(4),2013,231-233.
13. New Analytical Method Development and Validation of Capecitabine in Pure and Tablet Dosage Forms by UV Spectroscopy, International Journal of Medicine and Nanotechnology, Mednano Publications, 1(2), 2014, 48 - 53.

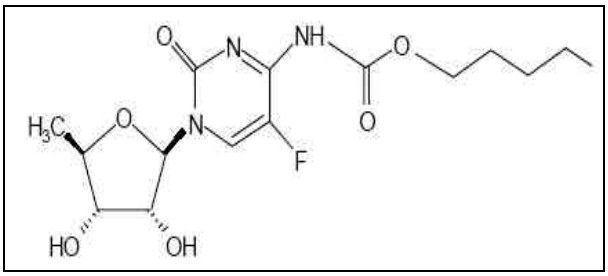

Figure.1.Structure of Capecitabine

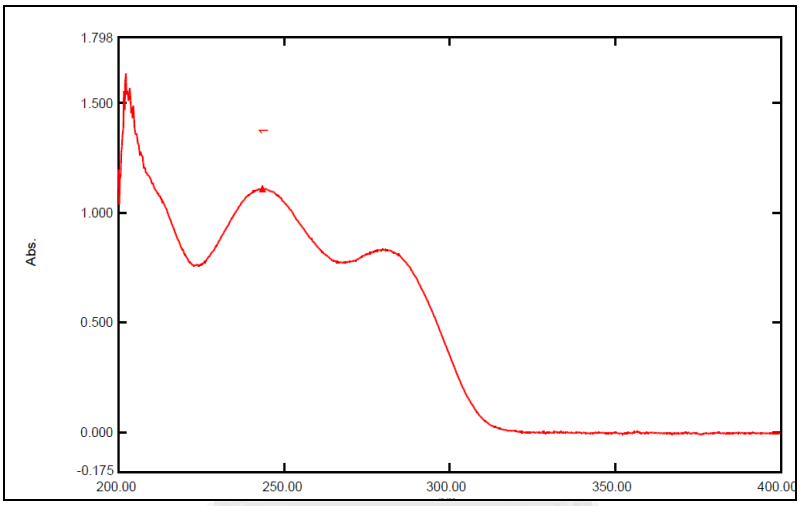

Figure.2. Absorbtion Spectra (ƛmax-243.60) Of 10µg/Ml Capecitabine

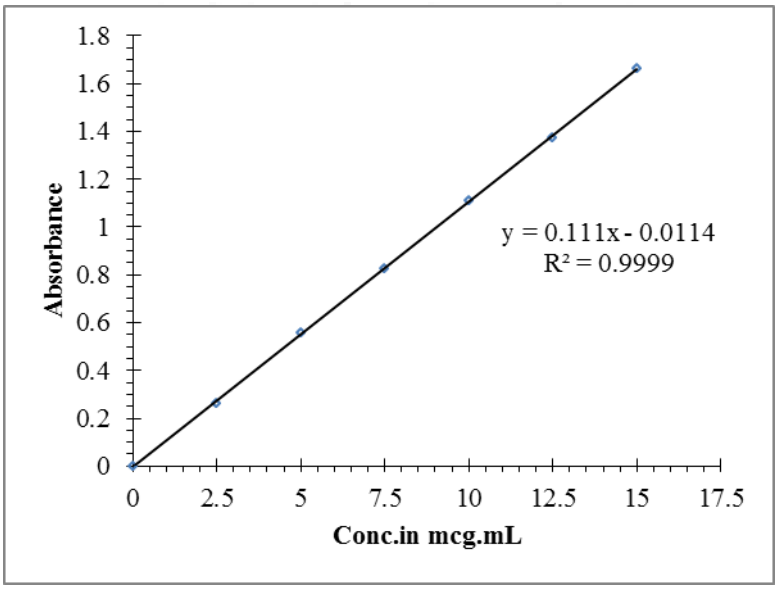

Figure.3. Linearity Graph of Capecatabibne

Table.1. Statistical Parameters for UV-Spectrophotometric Determination of Capecitabine

%	Conc	Area
0	0	**0**
25	2.5	0.261
50	5.0	0.555
75	7.5	0.824
100	10.0	1.108
125	12.5	1.375
150	15.0	1.664
Slope,b		**0.111**
Intercept,a		**0.0114**
Correlation,r2		**0.9999**
LOD		**0.177**
LOQ		**0.592**

Table.2: Precision Data for Capecitabine

S No	Name	ABS
1	Solution-1	1.11
2	Solution-2	1.109
3	Solution-3	1.102
4	Solution-4	1.11
5	Solution-5	1.092
6	Solution-6	1.096
Avg		1.103
Std Dev		0.00781
% RSD		0.71

Table.3: Accuracy Data for Capecitabine

Accuracy Level	50%	100%	150%
S No	Area	Area	Area
Injection-1	0.546	1.089	1.656
Injection-2	0.548	1.082	1.65
Injection-3	0.543	1.08	1.648
Avg	0.546	1.084	1.65133333
Amt. Recovered	50.17	99.30	151.82
%RSD			
%Recovery	100.34	99.30	101.22

Table.4: Ruggedness Data for Capecitabine

S No	Name	Analyst -1 RT	Analyst -2 RT
1	Scan-1	1.11	1.086
2	Scan-2	1.109	1.089
3	Scan-3	1.102	1.082
4	Scan-4	1.11	1.096
5	Scan-5	1.092	1.098
6	Scan-6	1.096	1.093
Avg		1.103	1.0906667
Std Dev		0.008	0.006121
% RSD		0.708	0.5612166

Table.5: % Assay of Market Brands of Capecitabine

Market Brand of the Drug	Taken in mg	Found in mg	% assay
Xeloda	500	499.95	99.99