ISSN NO. 2320-5407

Journal homepage:http://www.journalijar.com

INTERNATIONAL JOURNAL OF ADVANCED RESEARCH

RESEARCH ARTICLE

UV – SPECTROPHOTOMETRIC METHOD DEVELOPMENT AND VALIDATION OF ACAMPROSATE CALCIUM IN BULK AND TABLET DOSAGE FORM

Shah Megha*, Rohit Minal

Department of Quality Assurance, Pioneer Pharmacy Degree College, At & Post Sayajipura, Vadodara 390019, Gujarat, (INDIA).

Manuscript Info *Abstract*

Manuscript History:

Received: 11 December 2013
Final Accepted: 22 January 2014
Published Online: February 2014

Key words:
Acamprosate calcium, UV-Spectrophotometric method, Tablet dosage form.

Corresponding Author

Shah Megha

A simple, rapid, accurate, precise, and economical spectrophotometric method for estimation of Acamprosate calcium in tablet dosage form has been developed. Beer-Lambert's law was followed in the concentration range of 10-50µg/ml (r^2= 0.989). LOD and LOQ were found to be 0.183 µg/ml & 0.55 µg/ml respectively. The result of percentage recovery and placebo interference shows that the method was not affected by the presence of common excipients. The method was validated by determining its accuracy and precision which proved suitability of the developed method for the routine estimation of Acamprosate calcium in solid dosage form.

Copy Right, IJAR, 2013,all rights reserved

INTRODUCTION

Acamprosate (Calcium bis acetyl- homotaurine), a homotaurine derivative, a structural analogue of γ – aminobutyric acid and an upper analogue of taurine, is a relatively new drug used to prevent relapse in weaned alcoholics.[Besson, J et al. 1998] The drug is official in European Pharmacopeia 5.0 [European Pharmacopeia, 2005],British Pharmacopeia 2009[British Pharmacopeia 2009].To date, three medications - Disulfiram, naltrexone, and acamprosate - have been approved by the U.S. Food and Drug Administration (FDA) for treatment of alcohol dependence. Naltrexone and acamprosate are categorized as anti- craving drugs.Treating alcohol dependence usually consists of two phases: detoxification and rehabilitation. The initial detoxification stage deals with acute withdrawal symptoms. The later rehabilitation stage attempts to prevent relapse and develops a lifestyle compatible with long-term abstinence.After oral administration, few side- effects and adverse reactions have been observed, with nausea and diarrhoea being the most frequent. [Mason BJ. 2001]

Mechanism of Action

Acamprosate helps to modulate and normalize brain activity, particularly in the glutamate and gamma-aminobutyric neurotransmitter systems. It stabilizes the chemical balance in the brain that would otherwise be disrupted by alcoholism, possibly by antagonizing glutamatergic N- methyl-D- aspartate receptors and agonizing gamma-aminobutyric acid (GABA) type A receptors. [NDA Application 21-431 CAMPRAL]

Literature survey reveals that few analytical methods like spectrophotometric methods[Kiran A et al. 2013],capillary electrophoresis [Fabre H, Perrin C. 1999],RP-HPLC-MS/MS [Luo M, Qin Y-P, Yu Q, et al. 2007],RP-HPLC[Fang T, Shasha Z et al. 2009], LC/MS/MS [Rhee YS, Park JH, et al. 2008] ,several bio-analytical methods like quantifying acamprosate in beagle dog plasma using QTRAP- resolution system.[Zhou G, Wang C, et al]

MATERIALS

Shimadzu UV- Visible Spectrophotometer-1800 was used for all spectral measurements. Sample standard acamprosate calcium bulk drug was obtained from Sun Pharmaceuticals and Acamprol tablets were obtained from Baroda Pharma.

Solubility Criteria for Acamprosate Calcium

From Pharmacopoeial survey, acamprosate calcium is reported as freely soluble in water. [European Pharmacopeia 2005, British Pharmacopeia, 2009] Based on reported methods, phosphate buffer pH 6.8 and distilled water are used as vehicle for method development. [Kiran A et al. 2013]

The present article reflects use of hydrotropic agent such as Potassium di-hydrogen phosphate having a defined concentration (3 M) for enhancing the solubility of Acamprosate calcium and thereby developinga simple UV spectrophotometric method

.

EXPERIMENTAL METHOD

Preparation of Standard Stock Solution

An accurately weighed 25mg of acamprosate calcium was taken and diluted in 25ml of distilled water to get a concentration of 1000 ug/ ml and it is named as stock I. From the stock I, 10 ml of solution was taken and diluted in 50 ml 3 M KH_2PO_4 and the final volume was made upto mark with distilled water to get a concentration of 100 ug/ ml and it is named as stock II. From the stock II, various working standards were prepared by further dilution with distilled water. The solutions were scanned on spectrophotometer in UV range 200- 400nm. Acamprosate calcium showed absorbance maxima at 217 nm. The scanned spectrum is shown in the figure 2.

Preparation of Calibration curve

Working standard solutions with concentrations ranging from 10-50µg/ml were prepared from stock II solution. The calibration curve was plotted by taking concentration on x-axis and absorbance on y-axis. The curve showed linearity with correlation coefficient (r^2) 0.989, shown in figure 3.

Analysis of Marketed Formulation

The tablets were grinded to provide a homogeneous powder and a quantity equivalent to one tablet was weighed and transferred in to 100 mL dried volumetric flask, containing about 50 mL of 3M Potassium di-hydrogen phosphate and sonicated for 5 minutes with intermittent shaking made up to the volume with distilled water, mixed well and filtered. Further 1 mL of the solution is diluted to 100 mL with distilled water. The final sample solution was prepared in such a way to get a concentration of 13.32 ug/ml. Absorbance of the resulting solution was measured at 217nm (figure 4).

METHOD VALIDATION

As per the ICH Guidelines, method was validated for different parameters like Linearity, Precision, Limit of Detection, Limit of Quantification, and Accuracy. [ICH Q2A, 1994]

1. Linearity

The linearity study verifies that the sample solutions are in a concentration range where analyte response is linearly proportional to the concentration. Calibration curves were performed by analysis of working standard solutions prepared from the formulation with at least five different concentrations in the range between 3.3 µg / ml – 16.65 µg/ ml. The equation of the regression line for Acamprosate Calcium, $y = 0.0081x + 0.0115$ ($R^2 = 0.989$) shown in table 2.

2. Precision

The intra-day and inter-day variation for determination of Acamprosate calcium was carried out in the same day under same conditions and on different days and % RSD were calculated. The method was found to be precise due to low values of the %RSD as shown in table 3.

3. Accuracy (% Recovery)

Accuracy of the method was determined in terms of % recovery of standard. Recovery studies were carried out by addition of standard drug solution at the level of 50 %, 100 % and 150 % to the pre-analysed sample. In this method the known concentration standard drug was added to the assay sample. Three set for each concentration levels was prepared and the recovery was calculated with respect to the standard solutions. The accuracy results are shown in table 4.

4. Limit of Detection, Limit of Quantification

The limit of detection is defined as the lowest concentration of an analyte that an analytical process can reliably differentiate from background levels. The limit of quantification is defined as the lowest concentration of the standard curve that can be measured with an acceptable accuracy and precision. In this study, LOD and LOQ were based on the standard deviation of the response and the slope of the corresponding curve using the following equations: (table 5)

LOD = 3.3 σ / S **LOQ = 10 σ / S**

Where,

σ = standard deviation of absorbance of sample

S = slope of calibration curve

Results

Acamprosate calcium shows λ_{max}at 217nm and the linearity plot yielded a correlation co-efficient (R^2) of 0.989 over the Beer- Lambert's range of 10 – 50 ug / ml. the regression equation was found to be Y = 0.0032x + 0.0288. The developed method was found to be precise as the % RSD values for intra – day and inter – day were found to be less than 2%.

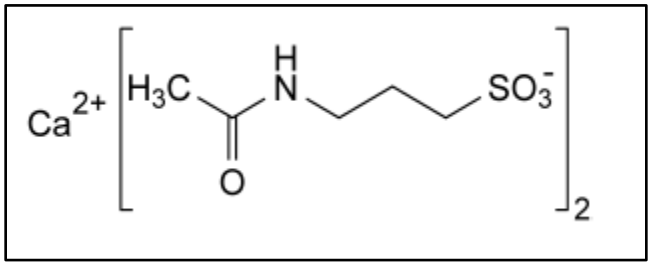

Fig 1. Molecular structure of acamprosate calcium

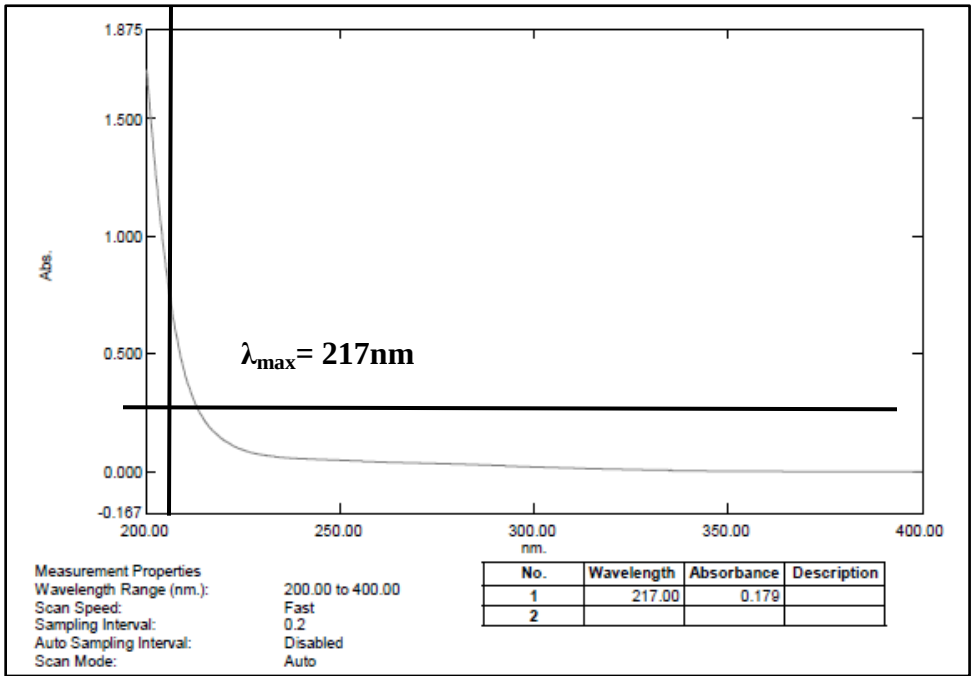

Fig 2. UV Spectrum of Acamprosate Calcium at 217 nm.

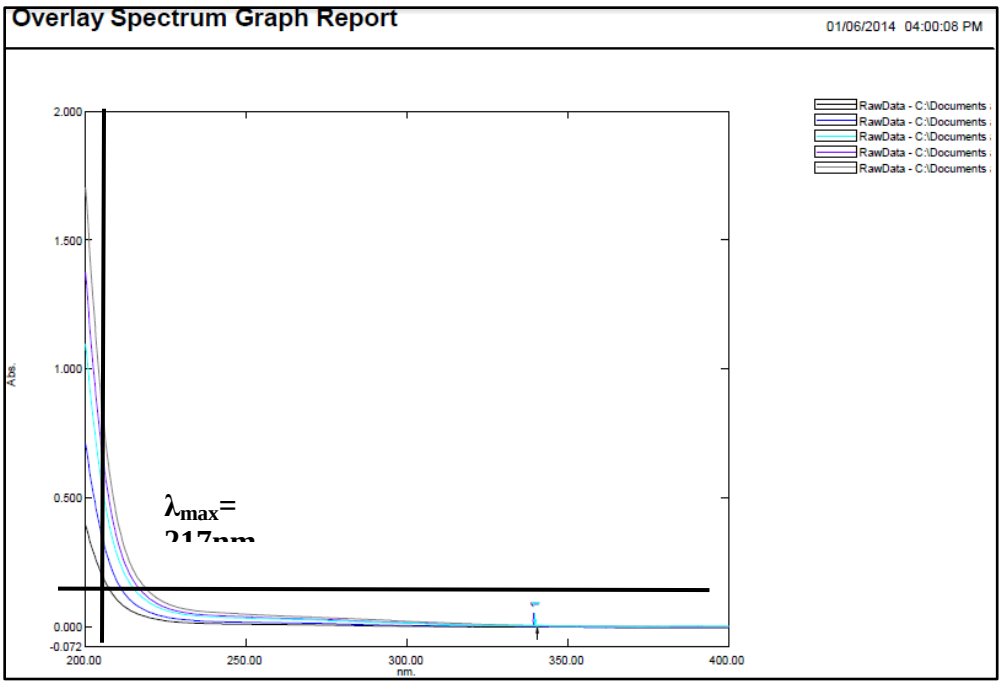

Fig 3. Calibration curve of Acamprosate calcium

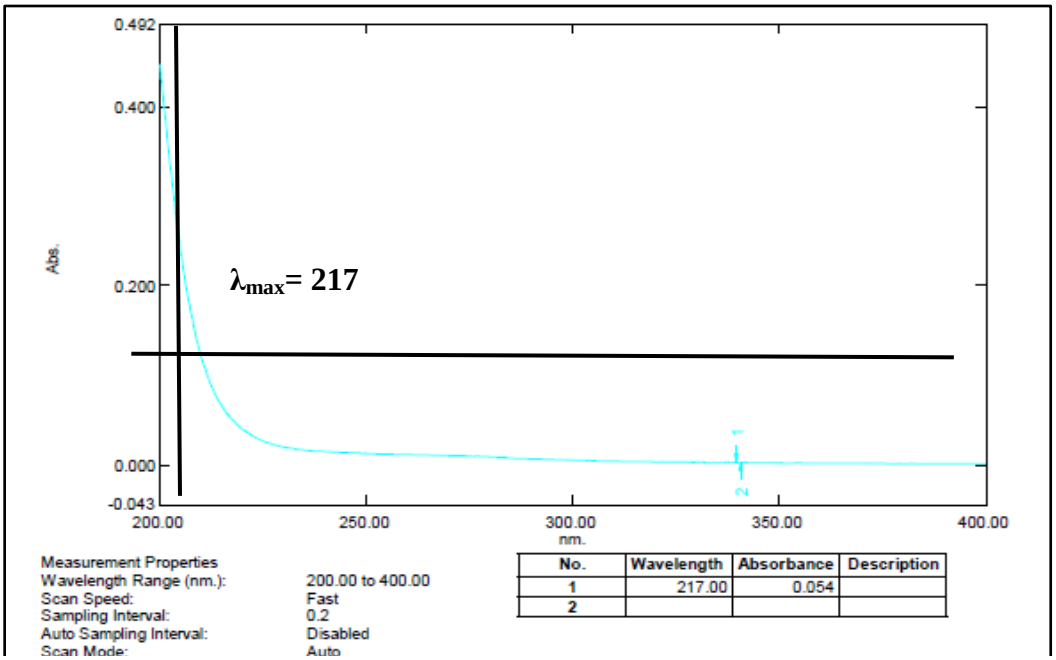

Fig 4: Sample Analysis of acamprosate calcium tablet

Table 1. Calibration curve of Acamprosate Calcium reported here

Concentration	Absorbance (217 nm)
10	0.049
20	0.077
30	0.124
40	0.146
50	0.179
Slope	0.003

Intercept	0.016
Regression Co-efficient (R^2)	0.989

Table 2. Linearity of Acamprosate Calcium

Concentration	Absorbance
3.3	0.019
6.6	0.027
9.9	0.038
13.32	0.044
16.65	0.051
Slope	0.0081
Regression co-efficient	0.0115
A Intercept	0.9899

Table 3. Results of Precision study (Intra- day and Inter- day)

Precision	Sample Concentration (ppm)	Obtained Concentration (ppm) (n=6)	% Relative Standard Deviation
Intra – day precision	13.32	12.36 12.36 12.33 12.33 12.33 12.33	0.13%
Inter- day precision	13.32	10 10 9.84 10 10 10	0.65%

Table 4. Recovery study of Acamprosate Calcium

Drug	% Amount added	Concentration added	Concentration Recovered	% Recovery	% Relative Standard Deviation
Acamprosate Calcium	80	9 9 9	6.95 6.95 6.99	77.22 77.22 77.66	0.33 %
	100	15 15 15	16.41 16.41 16.58	109.4 109.4 110.5	0.60%
	120	21 21 21	22.61 22.41 22.61	105.76 106.71 105.76	0.52%

Table 5. LOD and LOQ for Acamprosate Calcium

Limit of Detection	0.183 ug/ml
Limit of Quantification	0.55ug/ml

CONCLUSION

The proposed UV method was found to be simple, sensitive, accurate, precise, and linear which can be used in determination of acamprosate calcium in bulk and tablet dosage form. The method is economical, rapid and does not require any sophisticated instruments. Hence it can be effectively employed for routine quality control analysis of acamprosate calcium in bulk and in tablet dosage form.

REFERENCES

1. Besson, J et al. (1998), combined efficacy of acamprosate and disulfiram in the treatment of alcoholism: A controlled study. Alcoholism: Clinical and Experimental Research, vol22(3), 573–579.
2. European Pharmacopoeia 5.0, 2005, published on behalf of European Directorate for Quality of Medicines and Healthcare, 906.
3. British Pharmacopoeia 2009, Published by The Stationary Office on behalf of the Medicines and Healthcare products Regulatory Agent, I, 63 – 65.
4. Mason BJ (2001), Treatment of alcohol-dependent outpatients with acamprosate: a clinical review. J ClinPsychiatry, PubMed, vol 62 Suppl 20:42-48.
5. New Drug Application 21-431, CAMPRAL (acamprosate calcium) Delayed-Release Tablets, 5- 15.
6. Kiran A et al. (2013), Validated UV Spectrophotometric method development and stability studies of acamprosate calcium in bulk and tablet dosage form, International Journal of Pharm Tech Research, vol 5 (3), 1241-1246.
7. Fabre H, Perrin C (1999), Determination of homotaurine as impurity in acamprosate calcium by capillary zone electrophoresis, Journal of Chromatography A., vol 853 (1-2), 421-430.
8. Luo M, Qin Y-P, Yu Q, et al. (2007), Determination of acamprosate calcium in human plasma by RP-HPLCMS/MS, Chinese J New Drugs, vol 16, 163–166.
9. Fang T, Shasha Z et al. (2009), Determination of acamprosate calcium by RP- HPLC, China Pharmacist, vol 12.
10. Rhee YS, Park JH, et al. (2008), Analysis of acamprosate in beagle dog plasma by LC-MS-MS, Arch Pharm Res. vol 31 (8), 1035-1039.
11. Zhou G, Wang C, et al.Quantitation of Acamprosate in Dog Plasma Using API-5500 QTRAP System with High Resolution.
12. International Conference on Harmonization (ICH), Validation of analytical methods: Definitions and Terminology, ICH Q2A, 1994