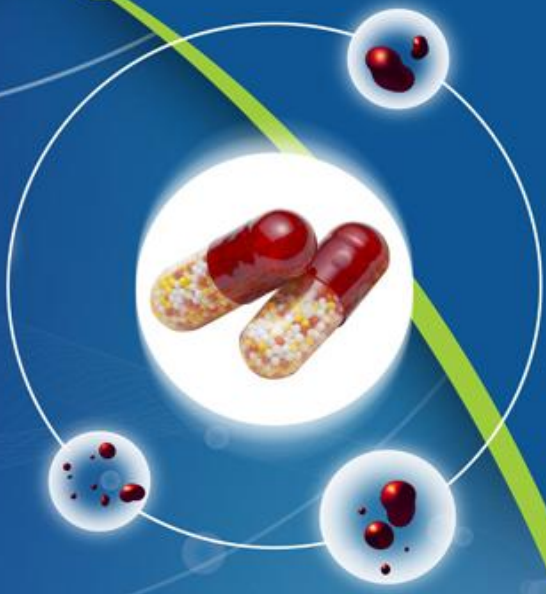
ISSN : 2320 4850

BI MONTHLY

Asian Journal of Pharmaceutical Research And Development

(An International Peer Reviewed Journal of Pharmaceutical Research and Development)



AJPRD

Volume - 02 Issue - 02 MAR-APR 2014

website: www.ajprd.com

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Asian Journal of Pharmaceutical Research and Development
(An International Peer-Reviewed Journal of Pharmaceutical Research and Development)
www.ajprd.com
ISSN 2320-4850

Research Article

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

K. V. Kandharkar, M. A. Nagras*

Quality Assurance Department, Sinhgad College of Pharmacy Pune, 411041, Vadgaon (Bk) Maharashtra, India,

***Received:* May 2014** ***Revised and Accepted:* May 2014**

ABSTRACT:

A simple, rapid, accurate, precise, specific 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 0.4 – 1.4 µg/ml (r2= 0.999). LOD and LOQ were found to be 0.013914 µg/ml 0.042614 µg/ml respectively. 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.

Key words: *Acamprosate calcium, UV- Spectrophotometric method, Tablet dosage form, Absorption maxima method*

INTRODUCTION:

Acamprosate Calcium Fig. 1 (Calcium bis acetyl- homotaurine), a homotaurine derivative, a structural analogue of γ – amino butyric acid and an upper analogue of taurine, is a relatively new drug used to prevent relapse in weaned alcoholics. The drug is official in European Pharmacopeia 5.0, 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 diarrhea being the most frequent.

*Corresponding author:
Assistant Professor
M. A. Nagras*
Quality Assurance Department,
Sinhgad College of Pharmacy
Vadgaon (Bk), **Pune, Maharashtra, India**

MATERIALS:

Shimadzu UV- Visible Spectrophotometer-1800 was used for all spectral measurements. Acamprosate calcium API and Distill Water, KH_2PO_4 buffer solution.

MECHANISM OF ACTION:

Acamprosate helps to modulate and normalize brain activity, particularly in the glutamate and gamma-amino butyric 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-amino butyric acid (GABA) type A receptors.

Literature survey reveals that few analytical methods are reported like spectrophotometric methods, capillary electrophoresis, RP-HPLC-MS/MS, RP-HPLC, and LC/MS/MS.

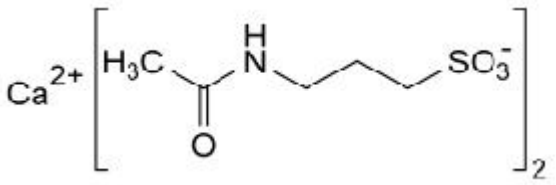

Fig 1: Molecular structure of Acamprosate calcium

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 of 3 M KH_2PO_4 and the final volume was made up to mark with distilled water quantity sufficient to 100ml to get a concentration of 100 ug/ ml and it is named as stock II. From the stock II, various working standards from 0.4 to 1.4 were prepared by further dilution with distilled water see table no. 1. The different solutions of concentration 0.4, 0.6, 0.8, 1.0, 1.2, 1.4 ppm 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.

Analysis of Marketed Formulation:

The tablets were grinded to provide a homogeneous powder and a quantity equivalent to 172.057mg 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 of 100 ml with distilled water quantity sufficient, mixed well and filtered through whatman filter paper no. 41. Further 0.1 ml of the solution is diluted to 10 ml with distilled water to get concentration of 10 ppm. Absorbance of the resulting solution was measured at 217nm (Figure 3).

Method Validation:

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

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 0.4 µg /ml – 1.4µg/ ml. The equation of the regression line for Acamprosate Calcium, y = 0.474x + 0.039 (R^2 = 0.999) as shown in Table 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.

Accuracy (% Recovery):

Accuracy of the method was determined in terms of % recovery of standard. Recovery studies were carried out by addition of standard drug (API) solution at the level of 80 %, 100 % and 120 % to the (Tablet) sample solution. Readings are taken in triplicate for each concentration levels 0.8, 1.0, 1.2 ppm and the recovery was calculated with respect to the standard solutions. The comparative accuracy results are shown in table 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 (SD) of the response and the slope of the corresponding curve using the following equations: table 5

$$\text{LOD} = \frac{\textbf{3.3 x SD of Y intercept}}{\textbf{Average of Slope}}$$

$$\text{LOQ} = \frac{\textbf{10 x SD of Y intercept}}{\textbf{Average of Slope}}$$

RESULTS:

Acamprosate calcium shows λ max at 217 nm and the linearity plot yielded a correlation co-efficient (R^2) of 0.999 over the Beer- Lambert's range of 0.4 – 1.4 ug / ml. The regression equation was found to be Y = 0.474x + 0.039. 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%. Recovery studies of Acamprosate calcium was carried out & % RSD found to be 0.80, 0.42, and 0.68 %.

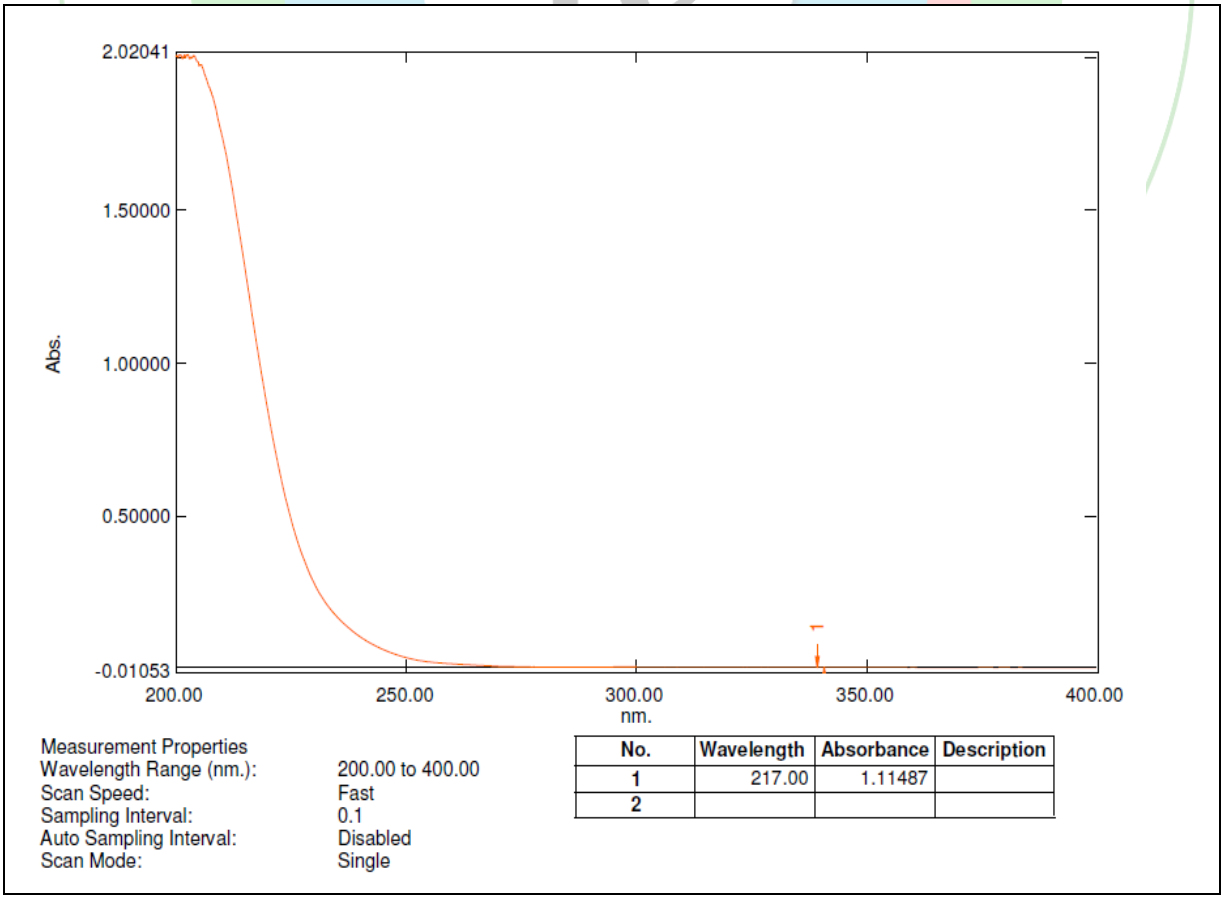

Fig: 2. UV Spectrum of Acamprosate Calcium (1 ppm) at 217 nm

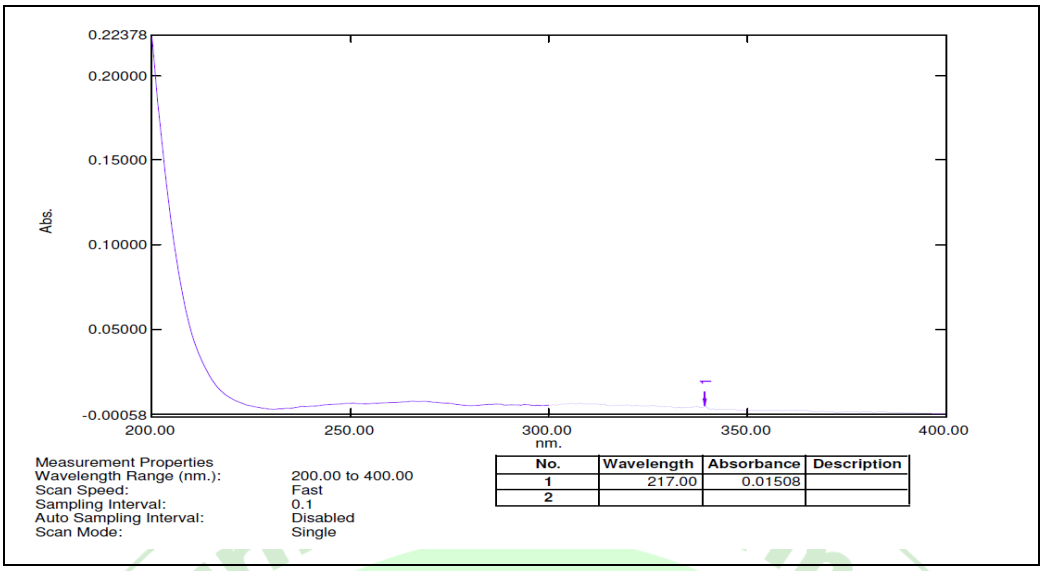

Fig: 3. Sample analysis of Acamprosate Calcium Tablet

Table: 1. Calibration curve for Acamprosate Calcium

Concentration	**Absorbance (217 nm)**
0.4	0.229
0.6	0.322
0.8	0.421
1	0.511
1.2	0.612
1.4	0.701
Intercept	0.039
Regression Co-efficient (R^2)	0.999

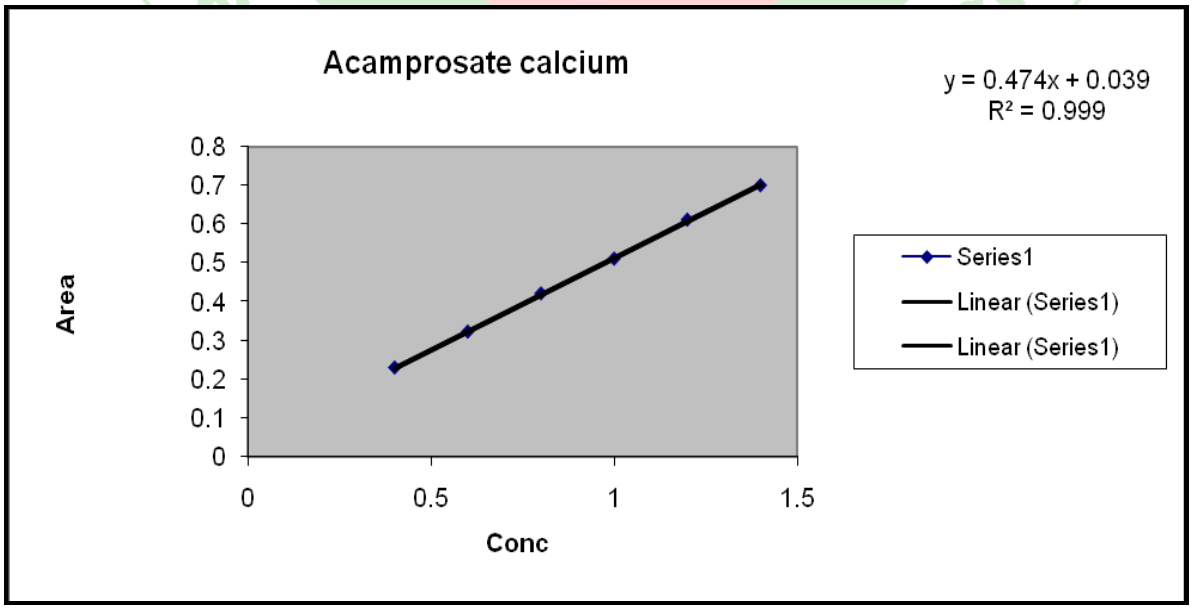

Fig: 4. Linearity of Acamprosate Calcium

Table: 2. Linearity of Acamprosate Calcium

Concentration	Absorbance
0.4	0.229
0.6	0.322
0.8	0.421
1	0.511
1.2	0.6121
1.4	0.701
Slope	0.474
Regression co-efficient	0.999
Y Intercept	0.039

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

Precision	Sample Concentration (ppm)	Obtained Concentration (ppm)	% Relative Standard Deviation
Intra – day precision	0.8	0.491	0.095879 %
	0.8	0.492	
	0.8	0.492	
	1.0	0.731	0.064458 %
	1.0	0.732	
	1.0	0.732	
	1.2	0.738	0.063934 %
	1.2	0.737	
	1.2	0.737	
Inter- day precision	0.8	0.491	0.33198 %
	0.8	0.493	
	0.8	0.489	
	1.0	0.730	0.171 %
	1.0	0.733	
	1.0	0.731	
	1.2	0.741	0.27766 %
	1.2	0.738	
	1.2	0.736	

Table: 4. Comparative Accuracy Study

API (Concentration in ppm) (n=3)	Absorbance	Acamprol Tab. (Concentration in ppm)	Absorbance
0.8	0.012	0.8	0.012
0.8	0.014	0.8	0.014
0.8	0.015	0.8	0.015
1.0	0.025	1.0	0.025
1.0	0.026	1.0	0.026
1.0	0.028	1.0	0.028
1.2	0.023	1.2	0.023
1.2	0.024	1.2	0.024
1.2	0.024	1.2	0.024

(n=3)

Table: 5. LOD and LOQ for Acamprosate Calcium

Limit of Detection	0.013914 µg/ml
Limit of Quantification	0.042614 µg/ml

Table no 6: Recovery study of Acamprosate Calcium

Drug	% Amount Added	Concentration Added (ppm)	Concentration Recovered	% Recovery	% Relative Standard Deviation
Acamprosate Calcium	80 %	0.8 0.8 0.8	0.805 0.7932 0.803	100.62 99.15 100.47	0.80
	100 %	1.0 1.0 1.0	0.995 1 0.9915	99.57 100 99.15	0.42
	120 %	1.2 1.2 1.2	0.612 0.608 0.616	100.73 100.035 100.416	0.68

(n=3)

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.

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