IJPSR (2011), Vol. 2, Issue 9 **(Research Article)**

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 30 May, 2011; received in revised form 15 August, 2011; accepted 23 August, 2011

ESTIMATION OF ORLISTAT BY UV SPECTROPHOTOMETRIC METHOD

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Keywords:

Orlistat,
Methanol,
UV spectrophotometer,
Validation

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ABSTRACT

A simple, reproducible and efficient spectroscopic method developed and validated for determination of Orlistat in bulk and capsule dosage form. The drug was determined spectrophotometrically at 203 nm using methanol as a solvent. The percentage recovery study of the drug for the proposed method ranges from 100.17-99.53%w/w indicating no interferences of the capsule excipients. Linearity was obtained in the concentration range 10-100µg/ml with correlation coefficient of 0.9982. The result analysis was validated statistically and recovery studies confirmed the accuracy and precision of the proposed method.

INTRODUCTION: Orlistat is an anti obesity drug [1], chemically it is (S)-((S)-1-((2S, 3S)-3-hexyl-4-oxooxetan-2-yl) tridecan-2-yl) 2-formamido-4-methylpentanoate, it works by inhibiting gastric and pancreatic lipases, the enzymes that break down triglycerides in the intestine. When lipase activity is blocked, triglycerides from the diet are not hydrolyzed into absorbable free fatty acids, and are excreted undigested instead. Only trace amounts of Orlistat are absorbed systemically; the primary effect is local lipase inhibition within the GI tract after an oral dose.

The primary route of elimination is through the feces [2-3]. Adverse drug reactions include faecal urgency and incontinence, flatulence, fatty stools or discharge, increased defecation; headache, anxiety, fatigue, menstrual irregularities; abdominal pain/discomfort. Drug interactions may decrease absorption of oral fat-soluble vitamins, amiodarone and propafenone may decrease plasma levels of cyclosporine. May alter the effects of warfarin may elevate plasma levels of pravastatin[4].

Literature survey has revealed that various methods have been reported for estimation of Orlistat in pharmaceutical formulations by RP-HPLC [5-6], LC-MS [7-8], GC-MS. No methods have been reported for estimation of Orlistat in pharmaceutical formulation by UV spectroscopy [9]. An attempt has been made to develop simple, economical and reliable method for determination of Orlistat in pure and pharmaceutical dosage form by UV spectrophotometric method.

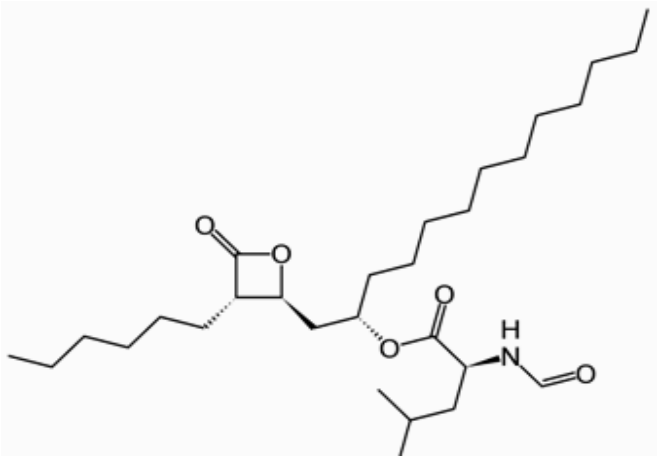

FIG. 1: STRUCTURE OF ORLISTAT

MATERIALS AND METHODS:

Instrumentation: Spectral and absorbance measurements were made using T60-UV-Visible spectrophotometer with soft ware UV win 5.0. 10mm path length quartz cells were used. Essae-Teraoka analytical balance was used for weighing.

Procedure:

Preparation of Standard Solutions: Accurately weighed 100mg of Orlistat was dissolved in few ml of methanol and the solution was diluted to 100ml to obtain a concentration of 1mg/ml. Further a 10ml solution was taken and again diluted to 100ml to obtain a standard stock solution of 100µgm/ml.

Preparation of Sample Solutions: Twenty capsules were opened, contents weighed and mixed. An aliquot of powder equivalent to 100mg Orlistat was accurately weighed and dissolved in 100ml of methanol and filtered. The filtered solution was further diluted to obtain a concentration of 100µgm/ml.

Proposed method for Orlistat: Aliquots of solutions 1-10ml are taken from the standard stock solution in to 10ml volumetric flasks. The volume is made up to 10 ml using methanol to obtain the concentrations of 10, 20, 30, 40…… 100 (µgm/ml). The absorbance was measured at 203nm against a blank. The calibration curve was plotted is given in **figure 2**. The spectrum for standard orlistat solution is given in **figure 3.**

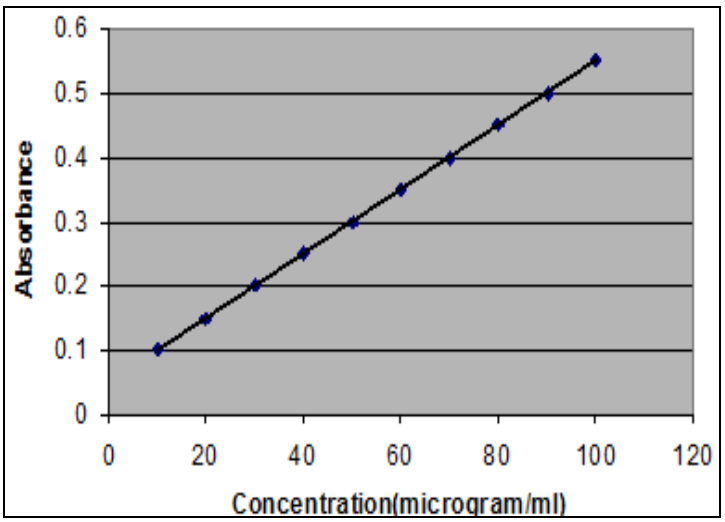

FIG. 2: CALIBRATION CURVE FOR ORLISTAT AT 203nm

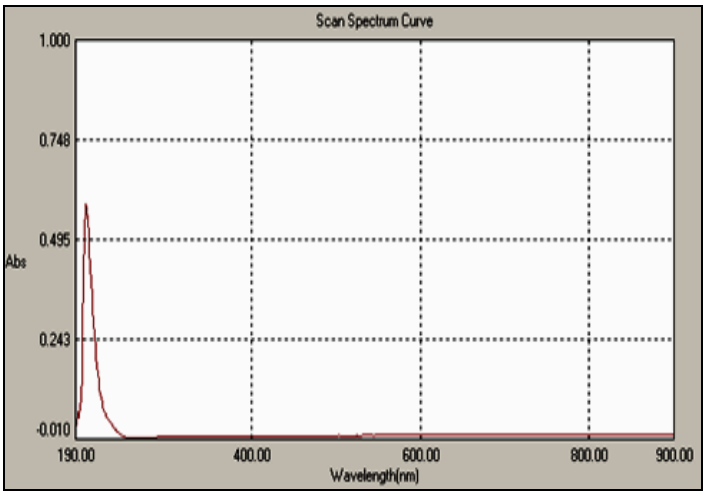

FIG. 3: SPECTRA OF STANDARD ORLISTAT SOLUTION

Method Validation: The proposed method was validated according to ICH Q2B guidelines for validation[10] of analytical procedures. The validation parameters determined are accuracy, precision, linearity, LOD and LOQ. The results are given in **table 1, 2 & 3.**

TABLE 1: ACCURACY

Concentration (µgm/ml)	% Amount found	Deviation
30	100.606	100.606±0.311
40	99.512	99.512±0.5134
60	100.0075	100.0075±0.7246

TABLE 2: PRECISION

Concentration (µgm/ml)	Standard deviation (SD)	%Relative standard deviation (%RSD)
30	0.311	1.03
40	0.5134	1.32
60	0.7246	1.20

TABLE 3: OPTICAL PARAMETERS

Parameters	
λmax	203nm
Beer's law limit (µgm/ml)	10-100
Sandell's sensitivity (µgm/cm^2/ 0.001 absorbance units)	0.132
Molar absorptivity (lit/mol.cm)	3.74x10^6
Regression equation (y= mx + c)	
Slope (m)	0.0049
Intercept (c)	0.1149
Correlation coefficient (r^2)	0.9982
%range of errors (confidence limits)*	
0.05 level	0.425
0.01 level	0.851
Limit of detection (LOD) (µgm/ml)	0.000485
Limit of quantification (LOQ) (µgm/ml)	0.00147

*Average of six determinants

Assay: The proposed method was applied to the determination of Orlistat in a brand name zero fat. The spectra obtained following the assay of zero fat capsules is given in **figure 4**. The result for assay is given in **Table 4.**

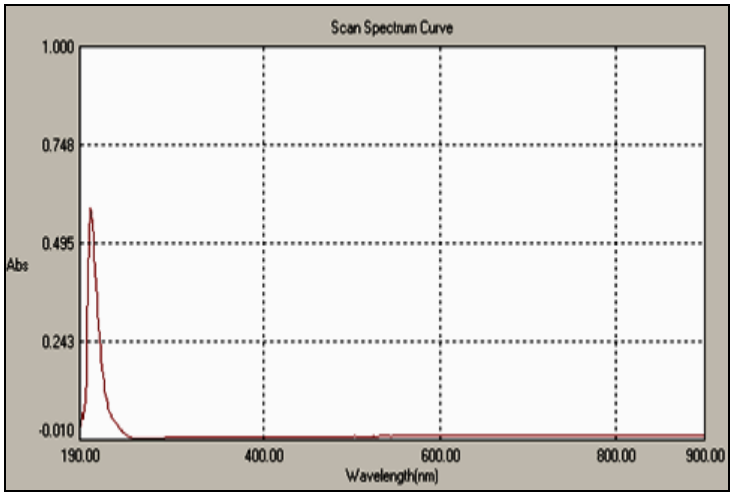

FIG. 4: SPECTRA OF SAMPLE ORLISTAT SOLUTION

TABLE 4: ASSAY

Sample	Labeled amount (mg)	Amount found (mg)	%Purity
Orlistat (Zero Fat)	120mg	119.82	99.85 ± 0.32

RESULTS AND DISCUSSION: In the proposed method linearity, assay, accuracy studies and precision were performed. The linearity was observed in the concentration range of 10-100µg/ml and correlation coefficient was found to be 0.9982. Results of accuracy studies are presented in Table 1. Percent recovery for orlistat was found in the range of 100.17 % to 99.53 %. The %R.S.D. for six determinations of sample was found to be less than 2.0 indicating the precision of the method. The method is selective as there is no interference from excipients present in capsule. The values for LOD and LOQ were found to be 0.000485 and 0.00147 respectively. The proposed method is simple, sensitive, accurate and precise and successfully applied for estimation of orlistat in capsule dosage form.

CONCLUSION: The proposed method was found to be simple, economical and sensitive. The statistical parameters clearly indicate the accuracy of the method. Analysis of the authentic samples containing showed no interference from common excipients. Hence this method could be considered for the determination of Orlistat in quality control laboratories.

ACKNOWLEDGEMENT: In the first place we would like to record our gratitude to Dr. R. Kamraj, M. Pharm, Ph. D., Principal, Greater Hyderabad Institute of Pharmacy, for extending his support.

Our sincere thank goes to Teaching, Non teaching and Technical staff of Greater Hyderabad Institute of Pharmacy, who helped in the successful completion of our work. We are also thankful to our dearest friend G. Avinash, for his help in completing our work.

Above all we are thankful to our dearest friends and Family members for their encouragement and support.

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