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Research Article

SPECTROPHOTOMETRIC METHODS FOR ESTIMATION OF NATEGLINIDE IN BULK DRUG AND ITS DOSAGE FORM

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ABSTRACT

Simple, accurate, precise, sensitive and highly selective spectrophotometric methods were developed for the estimation of Nateglinide. The estimation of Nateglinide was carried outby same solvent like phosphate buffer ph is 6.8(method I) at 239nm, (method II) at 248nm and (method III) at 217nm. And these methods were found to be linear in the range of 2-16µg/ml, for method I,2-12 for method- II and 2-16µg/ml for method III. And Beers law rangewere found to be 1-15µg/ml, 1-15µg/ml, and10-250µg/ml, and with mean recovery of 99.84 %, 99.45 % and 100.3 % of Nateglinide for methods I, II and III respectively. The developed method was validated according to ICH guidelines and it found to be accurate and precise Thus the proposed method can be successfully applied for simultaneous determination of Nateglinide and in routine analysis work.

Keywords: Nateglinide, Spectrophotometric, Validation, Beer's law.

INTRODUCTION

Nateglinide[1-3]chemically [N-(trans-4-isopropyl cyclo hexyl carbonyl)-D-phenylalanine] is a novel, nonsulfonyl urea derivative used for the treatment of type II diabetes mellitus[4-6]. It is used in novel drug delivery system[7] and In-vitro studies of drugs[8].It is not official in any Pharmacopoeia. Literature survey reveals that micellar electrokinetic chromatography(MEKC)[9],Spectrophotometric methods[10-15],HPLC[16-17],LiqidChromatography[18], HPTLC[19-20].In the present study, an attempt has been made to develop three different UV spectrophotometric methods for the determination of nateglinide in bulk and marketed formulations using phosphate buffer. ANOVA test was applied for comparison of both the methods. The developed methods were found to be simple, sensitive and reproducible.

MATERIALS AND METHODS

Instrumentation

The present work was carried out on ElicoSL164 UV- visible spectrophotometer having doublebeam detector configuration.The absorption spectra of reference and testsolution were carried out in a 1 cm quartz cell over the range of 200-800 nm.

Chemicals

All chemicals of analytical grade used as it is.

Preparation of standard solution

A stock solution of 1 mg/ml was prepared in phosphate buffer ph is 6.8. This solution is diluted with phosphate buffer ph is 6.8 to obtain required concentrations.

Preparation of sample solutions

20 tablets were weighed and powdered to 100mg of Nateglinide was weighted and transferred to

the 100ml volumetric flask. To it 50 ml of phosphate buffer was added and shake until the drug is dissolved.The solution was filtered and made up to100ml with phosphate buffer. This solution was suitably diluted to obtain the required concentration. The same in other methods with respective solvent.

PROCEDURE

Aliquots of working standard solution of Nateglinide 1-6ml (100µg/ml) were transferred into a series of 10ml volumetric flask. The volumetric flasks are made up to the volume with the same solvent phosphate ph is 6.8 (method-I), (method-II), (method-III).Then the absorbance of the samples are measured spectrophotometrically at 239nm for method-1 using phosphate buffer (ph-6.8) , at 248nm for method–II using phosphate buffer and at 415nm for method-III using phosphate buffer against a reagent blank.

VALIDATION

Validation of the developed method was done according to ICH guidelines[21-22]

Linearity

The linearity of the method is its ability to elicit test results that are directly proportional to the concentration of the analyte in samples. The calibration curve was taken in the range of 2-16 µg/mL, 2-12 at the respective λmax for method I,Method II,and 2-16 µg/ml for method-III. The correlation coefficient of the linearity were found for three methods and reported in table No.1

Precision and Accuracy

The precision of an analytical method is determined by assaying a sufficient number of aliquots of a homogeneous sample to be able to calculate statistically valid estimate of% Relative Standard Deviation (%RSD).Intermediate precision was done to express within laboratory variation, on different days. Five replicates of 10 µg/ml concentration of the working standard mixture and sample solution were analyzed %RSD was found to be less than 2%. Accuracy were determined for three methods and results were reported in table no.2.

Specificity

Results of tablet solution showed that there is no interference of the excipients when compare with the working standard solution. Thus, the method was said to be specific.

RESULT AND DISCUSSIONS

The optimum conditions for methods I, II and III have been established by varying the parameters one at a time and keeping the other parameters fixed and observing thee effects of products on the absorbance of the sample and colored species. Beer's law limits, molar absorbivity,Sandal's sensitivity, %range of error and % relative standard deviation are summarized in Table I. The regression analysis using the method of least squares was made for the slope (b), intercept(a) and correlation coefficient (r)obtained from different concentrations are given in Table I The results showed that these methods have reasonable precision. To evaluate the validity and reproducibility of the methods, known amounts of pure drug were added to the previously analyzed pharmaceutical dosage forms and the mixtures were analyzed by the proposed methods. The percentage recoveries are given in Table - 2. The interference studies veiled that the common excipients and other additives that are usually present in the injection dosage forms did not interfere at their regularly added levels.

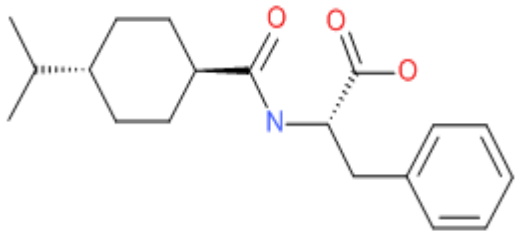

Fig. 1: Structure of Nateglinde

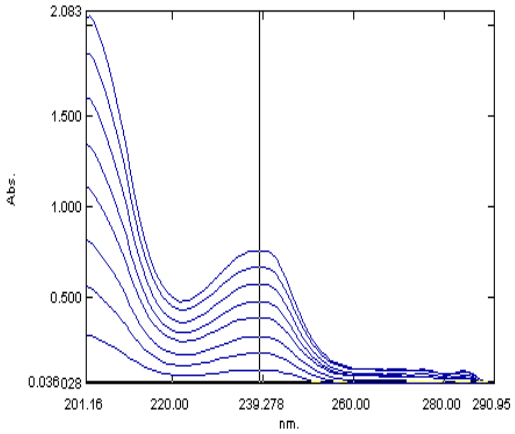

Fig. 2: Determination of Nateglinide by simple UV spectroscopy

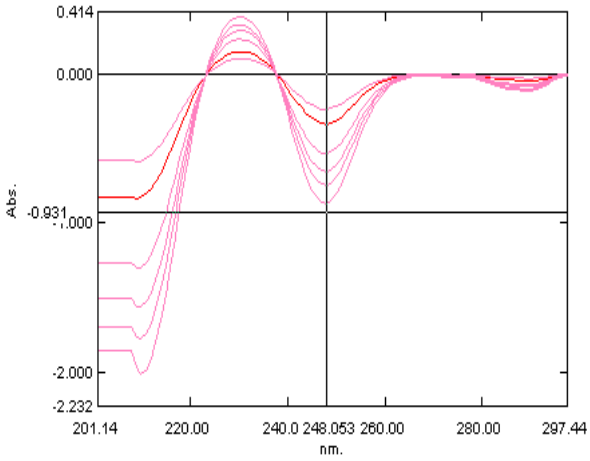

Fig. 3: Determination of Nateglinide by first order derivative spectrophotometric method

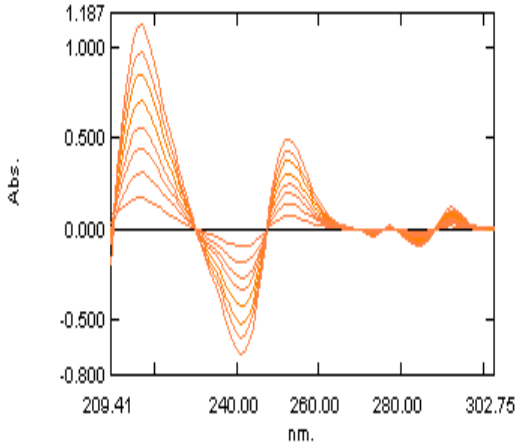

Fig. 4: Determination of Nateglinide by second order derivative spectrophotometry method

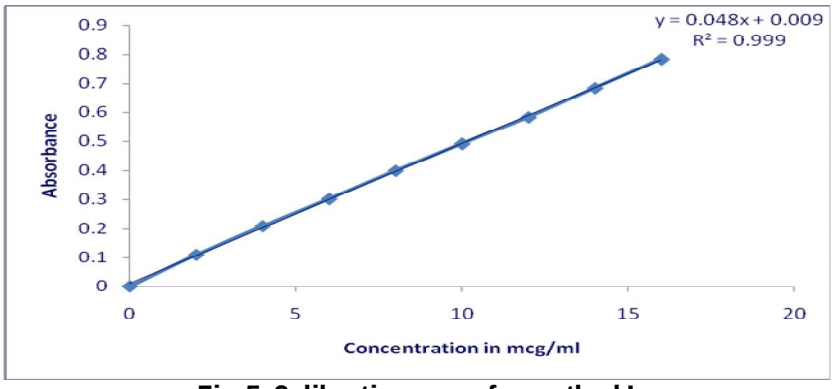

Fig. 5: Calibration curve for method I

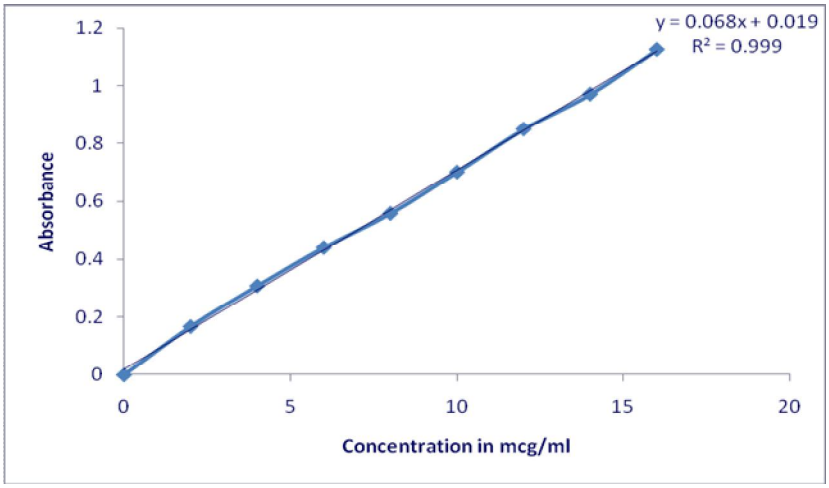

Fig. 6: Calibration curve for method II

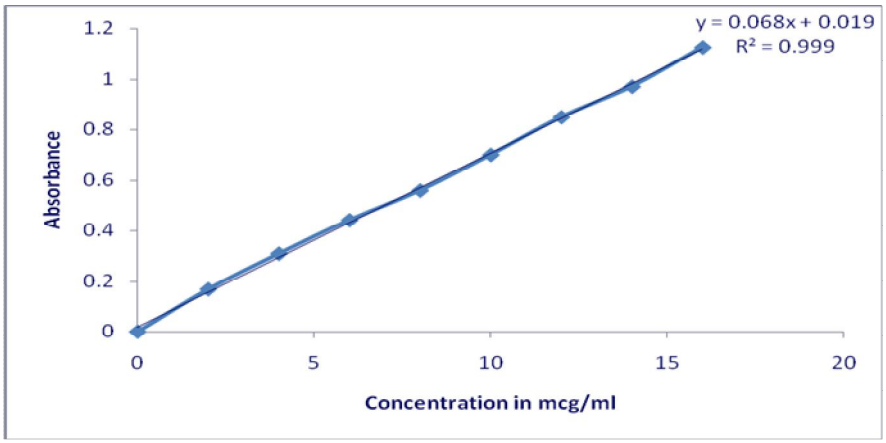

Fig. 7: Calibration curve for method III

Table 1: Optical regression characteristics, precision and accuracy of the proposed methods

Parameter	$Method_I$	$Method_{II}$	$Method_{III}$
λmax(nm)	239	248	217
Beer's law limits (µg.ml-1)	2-16	2-12	2-16
Molar absorbivity (lit . mole-1,cm-1)	$0.0492X10^4$	$0.0054X10^4$	$22.221X10^3$
Sandell's sensitivity (µg.cm-2/0.001 abs.unit)	0.020	0.018	0.014
Regression equation (y*=a+bx)	Y=0.048C+0.009	Y=0.053C+0.012	Y=0.068C+0.019
slope (b)	0.048	0.053	0.068
Intercept (a)	0.009	0.012	0.019
Correlation Co-efficient (r)	0.9999	0.998	0.999
RSD	0.648	0.313	0.713

Y = a+ bc where x is the concentration of Nateglinide µg/ml and Y is the absorbance at the respective λ max.

Table 2: Assay of Nateglinide in Pharmaceutical formulation

Formulation	Labeled amount in mg	Amount found by proposed $Method\text{-}M_I$	Amount found by proposed $Method\text{-}M_{II}$	Amount found by proposed $Method\text{-}M_{III}$	%Recovery* proposed by $Method\text{-}M_I$	%Recovery* proposed by methods $–M_{II}$	%Recovery* proposed by methods $–M_{III}$
Tablet-I	60	59.904	59.67	60.18	99.84	99.45	100.3

R. Reference was UV method developed in the lab
oratory.*Recovery amount is the average of six determinations.

CONCLUSIONS

The proposed spectrophotometric methods were accurate, precise and reliable for the measurement of SIM in dosage form. The developed spectrophotometric method was validated for estimation of SIM using linearity, range, accuracy and precision. The RSD for all parameters was found to be less than one, which indicates the validity of method and assay results obtained by this method are in fair agreement. The developed method can be used for routine quantitative estimation of SIM in pharmaceutical Preparation.

ACKNOWLEDGEMENTS

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