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Research Article

NEW EXTRACTIVE SPECTROPHOTOMETRIC ESTIMATION OF SITAGLIPTIN PHOSPHATE AND ITS DOSAGE FORMS

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Abstract: A simple, accurate, sensitive and reproducible visible extractive spectrophotometric method has been developed for the determination of Sitagliptin Phosphate (SGP) in bulk and also in pharmaceutical formulations. The proposed method is based on complexation of the drug with metanil yellow extracted with chloroform, showing absorbance maxima at 410 nm. Beer's law is obeyed over a concentration range of 25-250 µg/ml respectively. All the results were satistically evaluated. All the variables were studied to optimize the reaction conditions. No interference was observed in the presence of common pharmaceutical excipients. The validity of the methods was tested by analyzing the drug in its pharmaceutical preparations. Good recoveries were obtained. The developed method was successful for the determination of Sitagliptin Phosphate in various pharmaceutical preparations.

Key**words:** Visible spectrophotometric method, Metanil yellow & Molar Absorptivity.

Introduction

Sitagliptin Phosphate is chemically 7-[(3R)-3-Amino-1-oxo-4-(2,4,5 Trifluorophenyl) butyl]-5,6,7,8-Tetrahydo-3-(Trifluoromethyl)-1,2,4-Triazolo [4,3-a] pyrazine phosphate (1:1) monohydrate **(Figure 1)**. Sitagliptin Phosphate is the first and only prescription medication in a new class of oral antihyperglycemic agents, which enhance the body's own ability to lower blood glucose when it is elevated**.** The therapeutic combination in Type II is the use of the orally active Dipeptidyl Peptidase-4 (DPP - IV) inhibitors (1-3) like Sitagliptin Phosphate. It is an oral anti-diabetic drug (4-8) that helps to control blood sugar levels by regulating the levels of insulin in the body.

A survey of literature reveals that, the analytical methods reported for Sitagliptin Phosphate were based upon Spectrophotometry [9-12], HPLC [13,14] and other related analytical techniques like Tandem Mass Spectroscopy[15,16]. As highlighted earlier, the use of the above drug has become, very wide spread. Very few methods are reported based on visible spectrophotometry. The present article seeks to bridge this gap by developing a simple, sensitive, accurate, rapid and economical visible spectrophotometric method in the pure form and its tablet formulation as per ICH guidelines.

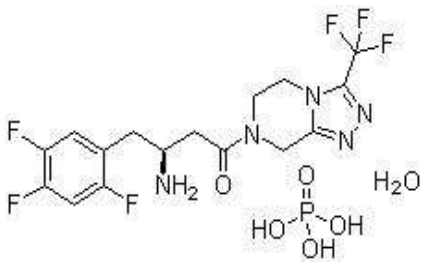

Figure 1:Structure of Sitagliptin: 7-[(3R)-3-Amino-1-oxo-4-(2, 4, 5 Trifluorophenyl) butyl]-5, 6, 7, 8-Tetrahydo-3-(Trifluoromethyl)-1, 2, 4-Triazolo [4, 3-a] pyrazine phosphate (1:1) monohydrate

Experimental

Instrument:

ELICO Double Beam UV-visible Spectrophotometer SL-244 with 1 cm matched pair quartz cells was used for all the spectral measurements.

Reagents:

Acid Phthalate Buffer pH 2.4, Metanil yellow (0.1%) , Chloroform AR grade , Hydrochloric Acid (0.2M) ,Methanol AR grade and Potassium Hydrogen Phthalate (0.2M). All the chemicals used were of analytical reagent grade. All the solutions were freshly prepared.

Procedure:

Preparation of Stock Solution

A standard stock solution containing 1 mg/ml was prepared by dissolving 100 mg of Sitagliptin Phosphate in 20 ml of methanol, shake well till it dissolves and make up to 100 ml with methanol.

Preparation of Working Standard Solution

From the above stock solution, working standard solution was prepared from 25-250 µg/ml.

Assay Procedure:

Aliquots of standard drug solution of Sitagliptin Phosphate containing 1 ml (25-250 µg/ml) were taken and transferred into series of separating funnel. To each solution 2 ml of metanil yellow, 2 ml of Phthalate buffer pH 2.4 and 5 ml of Chloroform were added. The solution is shaken for 2 to 3 minutes and kept aside for the formation of colored complex. The absorbance of the yellow colored chromogen was measured at 410 nm against reagent blank and a

calibration curve was constructed as depicted in **Figure 2.** The absorbance of the sample solution was measured, and the amount of the drug was determined by referring to the calibration curve.

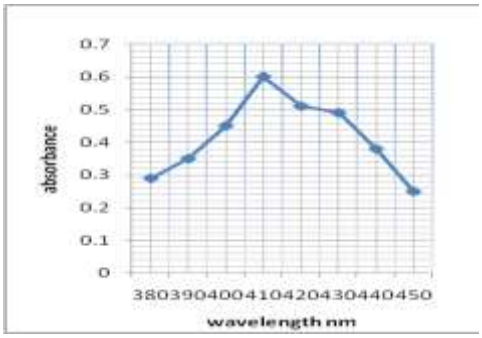

Figure 2: Absorption Spectrum of Sitagliptin Phosphate with Metanil yellow

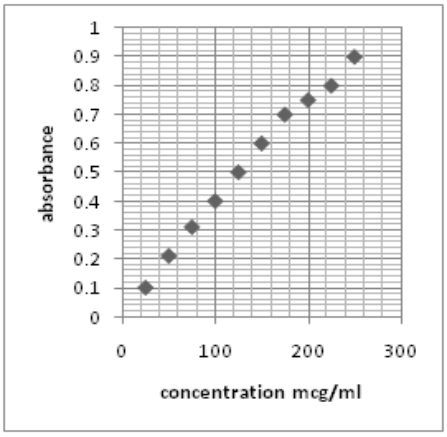

Figure 3: Linearity calibration curve of Sitagliptin Phosphate with Metanil yellow

Preparation Of The Sample Solution

Ten tablets of Sitagliptin Phosphate were accurately weighed and powdered. Tablet powder equivalent to 100 mg of Sitagliptin Phosphate was dissolved in 50 ml of methanol, sonicated for 15 mins and filtered. The filtrate is combined and the final volume was made to 100 ml with methanol. The solution was suitably diluted and analyzed as given under the assay procedure for bulk sample. The analysis procedure was repeated three times with Tablet formulations and the results of analysis for the method is shown in **Table: 1.**

Table 1: Assay of Sitagliptin Phosphate in Tablet Formulation

Tablet Formulation	Amount claim (mg / tablet)	*Amount Obtained (mg) by the propsed methods	** % Recovery by the proposed methods
1	100	98.6	98.6
2	100	99.2	99.2
3	100	102.8	102.8

* Average of Three determinations
** After spiking the sample

Recovery Studies

To ensure the accuracy and reproducibility of the results obtained, known concentration of the pure drug solution was added to the previously analyzed formulated solution samples and these samples were reanalyzed by the proposed method and also preformed recovery studies. The percentage recoveries, thus obtained for method is given in **Table: 1.**

Results and Discussion

The optimum conditions were established by varying one parameter at a time and keeping the others fixed and observing the effect on absorbance of chromogen. In the present work, the method is based on formation of chloroform extractable colored complexes with metanil yellow. The conditions required for the formation of colored complexes to form colored species were optimized.

Statistical analysis was carried out and the results were found to be satisfactory. Relative standard deviation values were low indicating the reproducibility of the proposed methods. Recovery studies were close to 100% that indicates the accuracy and precision of the proposed methods. The optical characteristics such as absorption maxima, Beer's law limits, molar absorptivity, Sandell's sensitivity and other parameters are presented in **Table: 2**

Table 2: Optical characteristics and precision data parameters for SitagliptinPhosphate

Parameter	Method
Measured λ_{max} (nm)	410
Beers law limit (µg/ml)	25-250
Moloar absorptivity (micrograms/cm^2/0.001 absorbance unit)	0.7431 x 10^5
Optimum photometric range (µg/ml)	30-100
Regression equation (y= mx + c)	Y=mx0.003522+0.0465
Intercept (c)	0.0461
Slope (m)	0.003522
Standard error of estimate	0.0524
Correlation coefficient (r)	0.9998
% RSD	1.03
Color stability (hours)	>2 hrs

Conclusion

This new procedure for the spectrophotometric determination of Sitagliptin Phosphate described in this work is simple, rapid and cost-effective with high accuracy and precision, when compared with previously reported procedures. It could find application as a convenient technique for the in-process control analysis of Sitagliptin Phosphate in bulk and its pharmaceutical formulations.

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