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Spectrophotometric determination of alogliptin in bulk and tablet dosage form using bromate–bromide mixture as brominating agent

A.V.V.N.K. Sunil Kumar [a], T.V. Reddy [b], C.B. Sekharan [c,*]

[a] *Department of Chemistry, NRI College, Vijayawada, India*

[b] *Department of Chemistry, Mallareddy College of Engineering, Secundrabad, India*

[c] *Department of Biochemistry, International Medical and Technological University, Dar Es Salaam, Tanzania*

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Abstract

Two simple and sensitive visible spectrophotometric methods (A and B) have been developed and validated for the determination of alogliptin in bulk and tablet dosage forms. The methods are based on the bromination of alogliptin using bromine produced by the action of HCl on the bromate–bromide mixture. The residual bromine is determined with a fixed amount of either methyl orange and measuring the absorbance at 505 nm (method A) or methylene blue and measuring the absorbance at 720 nm (method B). Linearity, accuracy and precision were found to be acceptable over the concentration ranges of 1–10 μg mL^{-1} and 2.5–12.5 μg mL^{-1} for method A and method B, respectively. The detection limits were 0.115 μg mL^{-1} and 0.210 μg mL^{-1} for method A and method B, respectively. The accuracy of the proposed methods was assessed by recovery studies and the percent recoveries of aloglitpin were found to be 99.91 ± 0.126%–99.99 ± 0.168% for method A and 99.86 ± 0.170%–99.98 ± 0.193% for method B. The methods were successfully applied to the determination of alogliptin in tablets with percentage recovery of 99.84 ± 0.139%–100.20 ± 0.625% (method A) and 99.96 ± 0.351%–10.320 ± 0.422% (method B). The optimized methods were fully validated and proved to be specific, robust, precise and accurate for the quality control of the alogliptin in their pharmaceutical formulations.

Keywords: Aloglitpin; Bromine; Methyl orange; Methylene blue; Tablets

1. Introduction

Alogliptin (AGN), chemically described as 2-[[6-[(3R)-3-aminopiperidin-1-yl]-3-methyl-2,4-dioxopyrimidin-1-yl] benzonitrile, is an oral antihyperglycemic agent. AGN belongs to dipeptidyl peptidase-4 inhibitor class and used in the treatment of type II diabetes milletus [1,2]. Usually dipeptidyl peptidase 4 degrades the glucagon like peptide 1 and incretins glucose-dependent insulinotropic polypeptide. The peptide 1 and polypeptide stimulate glucose dependent secretion of insulin, repress glucose dependent glucagon secretion, reducing food intake and gastric emptying. The inhibition of dipeptidyl peptidase 4 by AGN increases the quantity of

* Corresponding author.
E-mail address: balumphil@gmail.com (C.B. Sekharan).
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active plasma incretins and glucagon like peptide 1 that helps in glycemic control [3,4].

Spectrophotometry [5,6], HPLC [7–10] and HPTLC [11] methods have been reported for the quantification of AGN in combination with other drugs. A few analytical methods were proposed for the quantification of AGN alone. RP-HPLC [12–17] and HPTLC [18] methods have been described for the quantification of AGN in bulk and tablet dosage forms. HPLC-MS/MS [19] and UPLC-MS/MS [20] methods have been reported to measure plasma AGN concentration in monkey and rat, respectively. The reported methods are expensive, time consuming, require an expertise personnel and sophisticated HPLC techniques.

Spectrophotometric method of analysis is widely used in the estimation of drugs in pharmaceutical formulations owing to its simplicity, good sensitivity, cost effectiveness and easy availability. In the existing literature there are two reports regarding the use of UV spectrophotometry for the quantification of AGN in bulk and tablet dosage forms [21–23]. The UV spectrophotometric methods are simple but they suffer from lack of selectivity as they involve measurements at shorter wavelength [21–23]. However, an extensive survey of the literature revealed that there is only one colorimetric method available for the determination of AGN in pure form and tablet formulation. The method is based on the derivatization of AGN with 1,2-napthoquinone-4-sulfonic acid sodium in alkaline medium [24]. The reported colorimetric method is associated with drawback like less sensitivity and the method is not fully validated.

The present study describes two visible spectrophotometric methods (A and B) for the quantification of AGN in bulk and tablet dosage forms. The methods are based on bromination reaction using bromate–bromide mixture and the residual bromine was determined by using two dyes (methyl orange-method A; methylene blue-method B). The proposed methods can be used in laboratories where expensive and modern chromatography equipment is not available.

2. Experimental

2.1. Instrumentation

All spectrophotometric measurements were recorded with ELICO (Hyderabad, India) double beam model SL 159 digital spectrophotometer. One cm matched quartz cells were used for absorbance measurements.

2.2. Reagents and materials

Alogliptin was obtained as gifted sample (Rainbow Pharma Training Labs, Hyderabad, India) and used as received. Nesina tablets (labeled to contain 6.25 mg and 25 mg of AGN/tablet, Takeda Pharmaceuticals America, Inc., Deerfield) were purchased from the local pharmacy market.

All chemicals used were of analytical reagent grade and distilled water was used to prepare reagents.

2.2.1. Bromate–bromide mixture

Stock solution of $KBrO_3$–KBr (equivalent to 1 mg mL^{-1} $KBrO_3$) was prepared by dissolving accurately weighed 100 mg of $KBrO_3$ (Sd Fine-Chem Ltd., Mumbai, India) and 1 g of KBr (Sd Fine-Chem Ltd., Mumbai, India) in 30 mL of water and diluting to the mark in a 100 mL calibrated flask with the same solvent. This stock solution was diluted stepwise to get 10 μg mL^{-1} and 20 μg mL^{-1} $KBrO_3$ solutions for use in methods A and B, respectively.

2.2.2. Methyl orange solution (MO)

The MO stock solution (1 mg mL^{-1}) was prepared by dissolving accurately weighed 100 mg of methyl orange (Sd Fine-Chem Ltd., Mumbai, India) in 30 mL of water and diluting to the mark in a 100 mL calibrated flask with water and filtered. Working standard solution of MO (50 μg mL^{-1}) was prepared by further dilution of the stock MO solution with water.

2.2.3. Methylene blue solution (MB)

The MB stock solution (1 mg mL^{-1}) was prepared by dissolving accurately weighed 100 mg of MB (Qualigens Fine Chemicals, Mumbai, India) in water and diluting to the mark in a 100 mL calibrated flask and filtered. Working standard solution containing 40 μg mL^{-1} of MB was prepared by dilution of the MB stock solution with water.

2.2.4. Hydrochloric acid

5 M HCl was prepared by diluting 42 mL of 12 N HCl (Fisher Scientific, Mumbai, India) to 100 mL with distilled water in a 100 mL volumetric flask.

2.3. Alogliptin standard solutions

AGN stock standard solution (1 mg mL^{-1}) was prepared by dissolving 100 mg of AGN in 20 mL of methanol and then diluted to 100 mL with water in a 100 mL volumetric flask. Working standard solution containing

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