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Review Article

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ALOGLIPTIN BENZOATE: A REVIEW OF LIQUID CHROMATOGRAPHIC METHODS

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ABSTRACT

Alogliptin benzoate, a highly selective DPP-4 inhibitor for treating type-2 diabetes, is analyzed using different HPLC methods. An Agilent 1200 HPLC system with a Hypersil Gold Thermo Scientific C18 column is employed for bulk and dosage form estimation, using acetonitrile and ammonium carbonate buffer as the mobile phase. In RP-HPLC, a Finepak sil C18 column with a methanol:water mobile phase achieves chromatographic separation. Chiral HPLC employes a Lux cellulose 2 column with an ethanol and diethyl amine mobile phase. All methods exhibit excellent linearity, accuracy, precision, specificity, and robustness. The RP-HPLC method is deemed robust, accurate, and specific, utilizing a JASCO Quaternary gradient pump system. Chiral HPLC, utilizing a Lux cellulose 2 column, proves to be a simple, rapid, accurate, selective, and precise method. The developed HPLC methods provide comprehensive and efficient analyses for alogliptin benzoate in various applications.

Key words: Alogliptin benzoate, HPLC, RP-HPLC, Chiral HPLC.

INTRODUCTION

Alogliptin benzoate is an antidiabetic drug belong to the Dipeptidyl peptidase-4 (DPP-4) inhibitor class with a molecular formula $C_{25}H_{27}N_5O_4$ and IUPAC name 2-({6-[(3R)-3-aminopiperidin-1-yl]-3-methyl-2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl}methyl)benzonitrile; benzoic acid. It is orally administered[1]. It is a novel hypoglycemic drug stimulates glucose-dependent insulin release[2]. Chemically alogliptin is prepared as a benzoate salt and exists predominantly as R-enantiomers (>99%). It undergoes little or no chiral conversion *in-vivo* to the (S) – enantiomer[3]. Physically the salt form is a white to off-white crystalline powder with molecular weight of 339.391 g/mol.

Solubility

Alogliptin benzoate is considered Biopharmaceutics Classification System (BCS) Class I (high solubility, high permeability)
Orally soluble – dimethyl sulforide
Sparingly soluble – water, methanol
Slightly soluble – ethanol
Very slightly soluble – octanol, isopropyl acetate[4].

In present review, we have complied the published analytical method reports for determination of alogliptin benzoate in pharmaceuticals formulations.
This review paper focus on the analytical procedure available for the estimation of alogliptin benzoate by using liquid chromatographic methods such as HPLC, RP-HPLC, chiral HPLC[5].

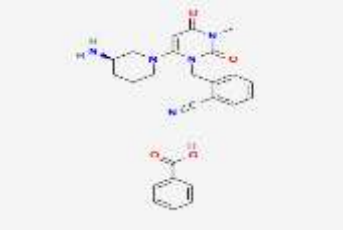

Fig.1: structure of alogliptin benzoate[4]

LIQUID CHROMATOGRAPHIC METHODS

HPLC

A new sensitive and rapid HPLC method was developed for the determination of alogliptin benzoate in bulk and pharmaceutical dosage forms; it was validated according to ICH and FDA guidelines[6,7]. The analysis was performed on the Agilent 1200 HPLC system.

Table 1: summary of methods related to HPLC.[8,9]

S. No.	Stationary Phase (Column)	Mobile Phase (with ratio)	Flow Rate	Detection Wavelength (λ)	Retention Time & Run Time	Validation Parameters (ICH & USFDA)
1	Hypersil Gold Thermo Scientific C18 (250 x 4.6 mm, 5 µm)	Mixture of Acetonitrile: Ammonium carbonate buffer (55:45 v/v)	1.0 mL/min.	277nm	4 min & 6.0 min.	LOD 0.03 µg LOQ 0.09 µg % RSD <2% Linearity range 85-306 µg/ml Regression equation Y= 17412x +1.1377 Regression coefficient (r^2) 1.00

RP-HPLC

A reversed-phase high performance liquid chromatographic (RP-HPLC) method has been developed for the determination of Alogliptin Benzoate based on isocratic elution using a mobile phase consisting of methanol: double distilled water (80:20, v/v) at a flow rate of 1 ml/min with UV detection at 222 nm. Chromatographic separation was achieved on a Finepak sil C18 column (250 mm × 4.6 mm, 5µm) by using JASCO Quaternary gradient pump system. It is equipped with four prominence LC Net II pump, and a UV – 2075 UV/Vis detector. Data acquisition was performed by using crome NAV software.

Table 2: Results obtained for RP-HPLC method for the determination of alogliptin benzoate in tablet[10-12]

Parameters	Results
Retention time	2.642
Wavelength of detection	222
Range of linearity	5-30 µg/ml
Regression equation	Y=24100x +35856
Regression coefficient(r^2)	0.998
Slope(m)	24100
Intercept(c)	35856
Precision Intraday %RSD Interday %RSD	 0.7345 0.3847
Accuracy	0.1537
LOD (µg/ml)	0.00137046
LOQ (µg/ml)	0.00415292

Chiral HPLC

An isocratic chiral stationary phase high-performance liquid chromatographic (CSP-HPLC) method has been developed and validated for the quantification of (S)-isomer in Alogliptin Benzoate. The chromatographic separation was achieved by using the 1200 series HPLC Agilent system consisted of quaternary gradient pump, auto sampler, column oven and a variable wavelength detector. The data can be monitored and integrated by using EZ-Chrom Elite Chromatography Data Software[13,14].

Table 3: summary of methods related to chiral HPLC technique.

S. No.	Stationary Phase (Column)	Mobile Phase (with ratio)	Flow Rate & Injection Volume	Detection Wavelength (λ)	Validation Parameters (ICH & USFDA)
1	Lux Cellulose-2 (250 mm x 4.6 mm, 5 µm)	Mixture of Ethanol: Diethyl amine (100: 0.5 v/v)	1.0 mL/min & 20µL.	230 nm	Correlation coefficient 0.9998 Calibration equation Y= 106716x +1302 LOD 0.0106 µg/ml LOQ 0.0345 µg/ml Precision (repeatability) 3.4% Intermediate precision 2.8% & 2.7% % RSD (S)-isomer spike level 0.25, 0.50, 0.75 :- 0.20 & 0.15 & 0.21.

CONCLUSION

The developed and validated methods of HPLC, RP-HPLC, Chiral HPLC was found to be more rapid, sensitive, linear, accurate, precise within all acceptable limits.

ABBREVIATIONS

DPP4 – Dipeptidyl peptidase.

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AUTHOR'S CONTRIBUTION

All authors made substantial contribution to the conceptualization, acquisition of data, methodology, validation, writing – review and editing.

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