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Short Communication

Different analytical methods for quantitative determination of alogliptin benzoate as a single drug either in a biological sample or pharmaceutical dosage forms

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ABSTRACT

This article discusses various analytical techniques for quantifying alogliptin benzoate in pharmaceutical dosage forms and biological fluids. Alogliptin is considered one of the recent antidiabetic drugs acting by inhibition of dipeptidyl peptidase-4 enzyme where exopeptidase cleaves N-terminal dipeptides from a range of substrates, including as cytokines, growth factors, neuropeptides, and incretin hormones. Different analytical techniques will be discussed, including spectrophotometric (UV-visible), spectrofluorimetric, chromatographic (thin layer chromatography, capillary electrophoresis, high-performance liquid chromatography), and electrochemical methods. The HPLC methods have been used to determine alogliptin benzoate in pharmaceutical dosage forms or biological fluids, while other spectrophotometric, spectrofluorimetric, TLC, and capillary electrophoresis methods have been applied for pharmaceutical dosage forms. These methods are validated according to ICH guidelines for linearity, range, limit of detection, limit of quantification, accuracy, and precision. Furthermore, there is a graphical comparison between the proportion of each technique.

Keywords: Diabetes, Alogliptin benzoate, quantitative analytical techniques, method validation.

1.Introduction

Diabetes is the ninth leading cause of mortality [1]. The health and quality of life of an individual are negatively impacted by diabetes. Given how healthy diabetes management affects patient fulfillment and overall quality of life, it has become crucial. Diabetes develops when the pancreatic beta cells cannot secrete enough insulin to regulate blood sugar levels within acceptable limits. There are two types of diabetes: type 1 diabetes, which is regarded as an autoimmune disease, and type 2 diabetes, which is characterized by erroneous proglucagon gene production. [2].There are many categories of oral antidiabetic drugs, such as sulfonylureas, meglitinides, biguanides, thiazolidines, α-Glucosidase inhibitors, dipeptidyl peptidase (DPP–4) inhibitors, and sodium-glucose transport protein 2 inhibitors [3]. They work by many mechanisms, including boosting insulin secretion, boosting muscle glucose uptake, boosting hepatic gluconeogenesis, boosting insulin sensitivity, reducing glucagon release, increasing satiation, reducing glucose reabsorption, decreasing glucose production, and reversing insulin resistance. They also work by reducing polysaccharide reabsorption, sucrose metabolism, glucagon release, and sucrose metabolism.[3,4]. The decision to use an oral antidiabetic drug is affected by many factors, including comorbidities, cardiovascular evaluation, and mortality [5].

Alogliptin is a (2-((6-((3R)-3-aminopiperidin-1-yl)-3-methyl-2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl) methyl) benzonitrile. Alogliptin benzoate (Figure 1) a. Its molecular weight is 461.5, and its molecular formula $C_{18}H_{21}N_5O_2.C_7H_6O_2$. It is a white powder, sparingly soluble in water and alcohol [6]. Alogliptin benzoate is an oral antidiabetic that acts by inhibition of the dipeptidyl peptidase enzyme (DPP 4), which is responsible for the degradation of glucagon-like peptide 1 (GLP-1) and incretins glucose-dependent insulinotropic polypeptide (GIP). Inhibition of DPP 4 increases the incretin level, which has a positive result on glycemic control. Moreover, inhibition of GIP and GLP-1 stimulates insulin secretion. Additionally, GLP-1 suppresses the release of glucose-dependent glucagon, induces satiety, lowers food intake, and slows stomach emptying rate. Alogliptin benzoate has an anti-inflammatory effect through inhibition of the production of the proinflammatory cytokines by toll-like receptor 4 (TLR-4)[7].

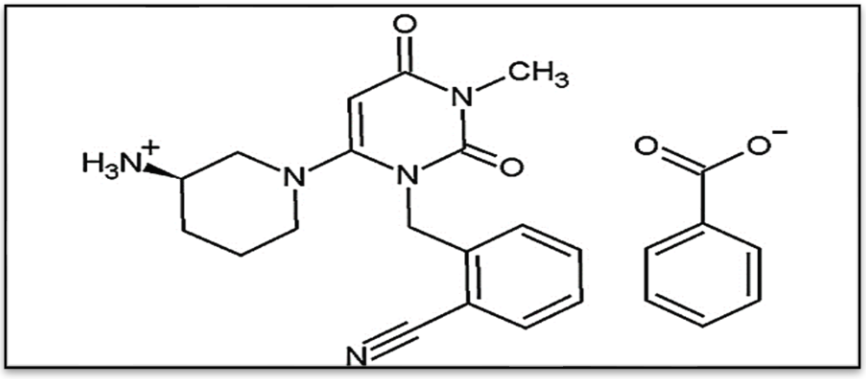

Figure 1. Chemical structure of Alogliptin benzoate.

This review has discussed different analytical methods for analyzing alogliptin, including spectrophotometric, spectrofluorimetric, electrochemical, capillary electrophoresis, and chromatographic methods.

2. Analytical methods

2.1 UV spectrophotometric methods

1. Colorimetric determination of alogliptin 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 or methylene blue and measuring the absorbance at 720 nm [8].
2. Colorimetric determination of alogliptin based on the reaction of alogliptin with picric acid or 2,4 dinitrophenol in the chloroform medium. The formed complex showed λ_{max} at 415 and 430 nm, respectively [9].
3. UV spectrophotometric determination of alogliptin by measuring the amplitudes at 278 nm for the first-order derivative spectra [10].

2.2. Spectrofluorimetric methods

Alogliptin does not have a native fluorescence activity, so the spectrofluorimetric methods depend on alogliptin's derivatization or quenching effect.

1.Spectrofluorimetric determination of alogliptin upon derivatization by 4-chloro-7-nitrobenzofurazan (NBD-Cl) in borate buffer at pH 8.5 to produce a strong fluorescent compound having excitation and emission wavelengths 470 and 527 nm [11].

2.Spectrofluorimetric determination of alogliptin based on the Hantzsch reaction produces a yellowish luminous compound with excitation and emission wavelengths 415 and 480 nm [12].

3.Spectrofluorimetric determination of alogliptin upon reaction with fluorescamine in slightly alkaline, having excitation and emission wavelengths 387 and 477 nm [13].

4.Spectrofluorimetric determination of alogliptin by measuring the quenching action of alogliptin benzoate on the eosin Y native fluorescence was measured at acidic medium pH: 3.5, having excitation and emission wavelengths 260 and 541 nm [14].

2.3. Chromatographic methods

2.3.1. Thin layer chromatography

Table 1. Different TLC methods used for the determination of alogliptin benzoate.

Stationary phase	**Mobile phase**	**Detector**	**Ref.no.**
silica gel 60F254	Acetonitrile: 1% ammonium acetate in methanol (4.5:5.5 v/v)	UV at 277 nm	[15]
silica gel 60F254	Benzene: Ethyl acetate: Triethylamine (7.5: 2: 0.5, v/v/v)	UV at 222 nm	[16]
silica gel 60F254	chloroform: methanol: ethyl acetate: triethyl amine, (9:1:1:0.5, v/v/v/v)	UV at 278 nm	[17]

2.3.2. Capillary electrophoresis

Capillary electrophoresis determination of alogliptin enantiomers on Untreated fused silica capillaries using different buffer solutions and detection at 200nm [18].

2.3.3. High-performance liquid chromatography.

Table 2. Different HPLC methods used for the determination of alogliptin benzoate.

Matrix	Column	Mobile phase	Detector	Ref.no.
Alogliptin and its potential impurities in pharmaceutical dosage form	Angilent Zobax SB-CN	Gradient elution of water: acetonitrile: trifluoroacetic acid 1900:100:1, by volume and acetonitrile: water: trifluoroacetic acid 1900:100:1, by volume	UV at 278 nm	[19]
Pharmaceutical dosage form	Hypersil Gold Thermo Scientific C18	Acetonitrile: ammonium carbonate buffer (55: 45, v/v)	UV at 277 nm	[20]
Human plasma	Thermo Hypersil ODS C18	50 mM phosphate buffer (pH = 2.5): acetonitrile (70: 30, v/v).	UV at 210 nm	[21]
(S)-isomer in Alogliptin benzoate in pharmaceutical dosage form	Lux cellulose	Ethanol and TEA (100:0.5v/v)	UV at 230 nm	[22]
Aloglitin in formulations and rat plasma.	Phenomenex Lux Cellulose-2	Methanol: 0.01% formic acid buffer pH 3 (70: 30 v/v)	UV at 230 nm	[23]
Pharmaceutical dosage form	Shiesdo	Water: methanol (25:75v/v)	UV at 225 nm	[24]
Alogliptin and its	Kromasil CN	Water: methanol (55:45, v/v)	MS	[25]

potential impurities in pharmaceutical dosage form				
Pharmaceutical dosage form	Zorbax SB-AQ	0.1% TFA in water: acetonitrile (62: 38, v/v)	UV at 295 nm	[26]
Pharmaceutical dosage form	Symmetry cyanide	Phosphate buffer pH (4.6)-acetonitrile (20:80, v/v)	UV at 215 nm	[27]
Alogliptin and its related impurities in pharmaceutical dosage form	Kromasil C18	Gradient elution of 0.1% perchloric acid pH 3 and acetonitrile	UV at 224 nm	[28]
Alogliptin and its process related substances in pharmaceutical dosage form	Phenomenex Gemini-NX C18	Gradient elution of ammonium acetate in water: acetonitrile and methanol (60:40, v/v)	MS	[29]
Human plasma	Symmetry shield C18	0.3% formic acid: acetonitrile (20: 80, v/v)	MS	[30]

2.4. Electrochemical methods

Only one electrochemical method has been applied for the determination of alogliptin benzoate using modified carbon paste electrode fabrication ($ZNCr_2O_4$ @MWCNTS /CPE) [31]

3. Conclusion

According to the collective literature for alogliptin benzoate, different methods can be used to determine alogliptin benzoate in its pharmaceutical dosage form or plasma. These methods are spectrophotometric, spectrofluorimetric, chromatographic, and electrochemical, as shown in Figure 2. The chromatographic techniques ranged from thin-layer

chromatography, capillary electrophoresis, and high-performance liquid chromatography, Figure 3. The chromatographic methods were more applicable for human plasma, while other methods were used for pharmaceutical dosage forms.

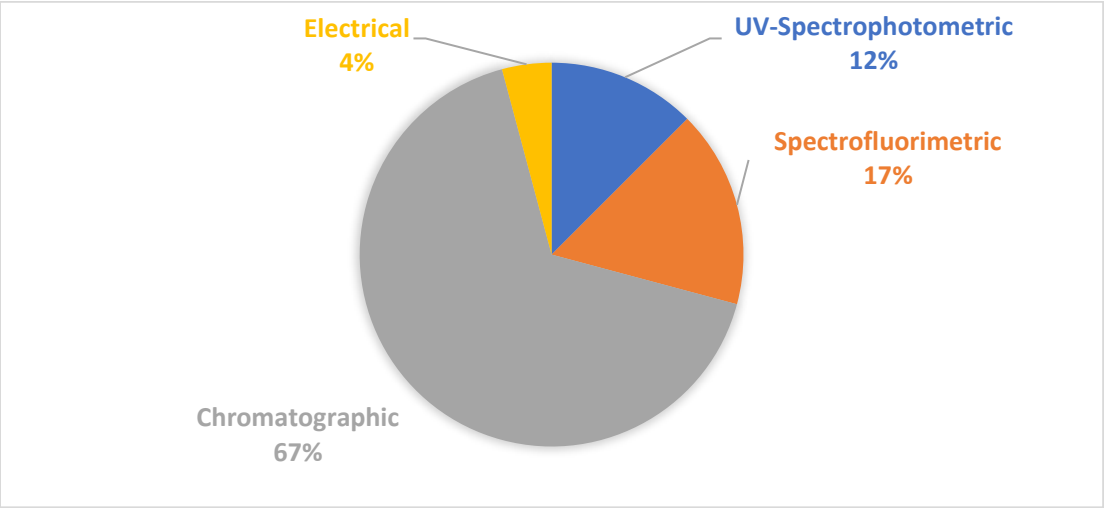

Figure 2. Percentage of each analytical method for determination of alogliptin benzoate.

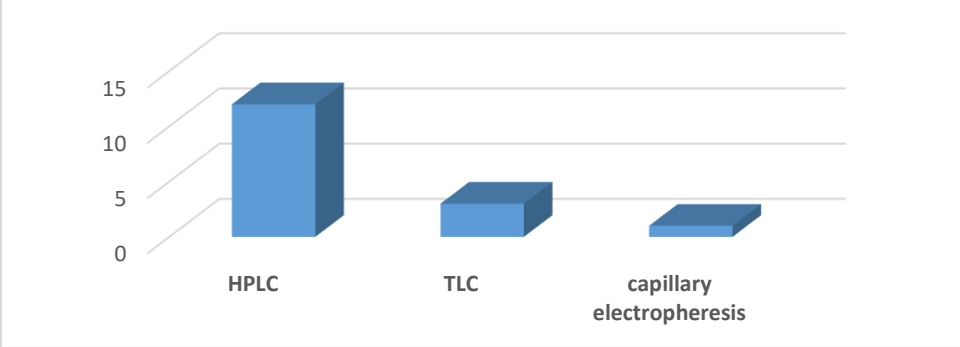

Figure 3. Different chromatographic methods used for the determination of aloglitin benzoate.

Conflict of Interest

The authors declare no conflict of interest.

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