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Research Article

HYDROTROPIC TECHNIQUE ASSISTED UV-SPECTROPHOTOMETRIC METHOD DEVELOPMENT AND VALIDATION FOR LINAGLIPTIN IN BULK AND PHARMACEUTICAL DOSAGE FORM

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ABSTRACT
Linagliptin (LGPTN), a DPP-4 antagonist variants, has antidiabetic effects. DPP-4 antagonists are an unconventional approach to type 2 diabetes treatment that promotes glucose-dependent insulin production while lowering glucagon amount by hindering the deactivation procedure regarding incretins, especially Glucagon Like Peptide 1 (GLP 1) & Gastric Inhibitory Polypeptide (GIP), resulting in developed glycemic control. The present research established a discriminate, comprehensive, cost-effective, & sensitive hydrotropic agent-assisted spectroscopy method that utilizes 1M urea (50:50% v/v) & 1M sodium bicarbonate for enhancement of dispersibility of less water-miscible LGPTN for estimating its amount in bulk and also in pharmaceutical dosage formulation. Absorption maxima identified at 272.5nm, although urea, sodium bicarbonate, along with other excipients did not possess any absorbance above 216nm, without any disruption in the investigation. At doses ranging from 10 to 60 µg/ml, LGPTN followed Beer's rule. The suggested strategy was checked against ICH recommendations, and the precision, accuracy, and also other statistical analysis values were obtained in good alignment with respect to required values, having a correlation coefficient of 0.9998. LGPTN recovery with respect to time in medicinal doses varied from 99.9 to 100.1%. The outcomes of analysis for precision, LOD, LOQ, & accuracy were excellent. The proposed method is easy, fast, and also ideal for quality control inspections regularly.

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Introduction

The molecular name for linagliptin (LGPTN) 8-[(3R)-3-Amino-1-piperidinyl]-7-(2-butin-1-yl)-3-methyl-1-[(4-methyl-2-chinazolinyl) methyl]-3, 7-dihydro-1H-purin-2, 6-dion. DPP-4 antagonists are an emerging strategy for treatment of type 2 diabetes that promotes glucose-dependent insulin secretion while lowering glucagon amounts through reducing the procedure of deactivating incretins, particularly Glucagon Like Peptide 1 (GLP 1) and Gastric Inhibitory Polypeptide (GIP), developing glycemic controls. The chemical structure of LGPTN is illustrated in **Fig. 1** [1].

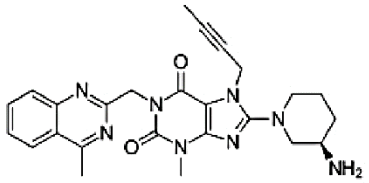

Fig. 1: Chemical structure of LGPTN

LGPTN, essentially not soluble in water. Therefore, hydrotropic chemicals are employed to enhance its water solubility [2-4]. The most widely used hydrotropic agents are urea & sodium bicarbonate. The hydrotropic solubilization technique increased the solubility of many poorly water-soluble drugs. A literature analysis discovered that HPLC, densitometric, spectrofluorimetric, and colorimetric methods have been reported to quantify LGPTN in pharmaceutical dosage formulations [5-8]. To excellence of our thoughts, there are not reported any work in the literature with regards to this Spectrophotometry technique for assessment of LGPTN using hydrotropic agents. As an outcome, it may considered to be useful for utilizing these hydrotropic solutions for extracting the medication from fine powder tablets in order to do spectrophotometer quantification.

Methodology

Instrumentation

Spectrophotometer employed was a double beam UV-visible spectrophotometer with a 10mm matched quartz cell.

Model: UV-1700 PHARMASPEC**.** Shimadzu, Japan

Analytical balance: Shimadzu, Japan AX 200.

Reagent & Chemical

Each chemical along with reagent solutions utilized were AR grade. LGPTN (API) was brought over as a gift sample from Aurobindo Pharma Pvt. Ltd, and the drug formulation was acquired in the local market, independently.

Method development

Standard Stock Solution (SSS) Preparation and Calibration Curve (CC):

To prepare a SSS of 100 µg/ml of LGPTN, a combination of hydrotropic sodium

bicarbonate and urea was used. An appropriate dilution of this stock solution was prepared & analyzed in UV range 200-400 nm. Wavelength of absorption of LGPTN was measured at 294nm. LGPTN's solubility increased by greater than 16 times with respect to mixed hydrotropic solution versus pure water. This enhanced solubility of LGPTN is because of hydrotropic solubilization mechanism [9-12]. Aliquots with 10 to 60 µg/ml were made incorporating exact solvent and also analyzed employing for absorbance at 294 nanometre in photometric mode **(Fig. 2)**. CC was created by graphing absorbance & the standard solution concentration on the Y-axis & X-axis respectively **(Fig. 2)**. This process has been implemented for the test sample solution and determined for being suitable to analyze the dosage forms denoted in **Table 2**.

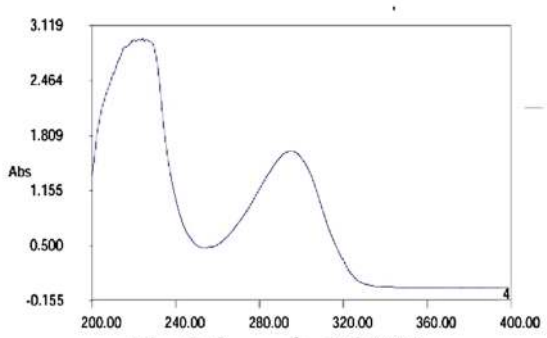

Fig. 2: λmax for LGPTN

Method validation

This approach was verified for criterions such as accuracy, precision, & linearity.

Linearity

Aliquots of stock solution (100 µg/ml) ranges within 10 to 60 µg. All materials were scrutinized in an UV-Visible spectrophotometer, employing 1M Sodium Bicarbonate ($NaHCO_3$) & 1M urea ($CO(NH_2)_2$) in water as control [13]. LGPTN showed linearity between 10-60 µg/ml **(Table 3)**.

Accuracy

The method's reliability was determined by comparing recovery rates at three distinct concentrations for 80, 100, and 120% of the samples. A reference drug solution was mixed into a previously tested sample solution, and the percentage of drug content was estimated [14-16]. Table 3 highlights the accuracy study results.

% Recovery = [(ct-cu)/ca] x 100,

ct = total concentration of the discovered analyte

cu = concentration of the analyte in the formulation

ca = strength of pure medication in addition to the formulation

Precision

Intra-day precision was being determined through running 5 distinct LGPTN test sample. The inter-day precision was also assessed on 2 separate analyzers on different days [17]. %RSD and test results obtained by the two analysts were adequate **(Table 4)**.

Results & Discussion

The recommended method's optical characteristics **(Table 1)** demonstrated that LGPTN had a λmax of 294 nm in a solvent-based mixture of 1M sodium bicarbonate and 1M urea having a correlation coefficient of 0.9999. Percentage purity along with obtained Relative Standard Deviation (%RSD) from the assay for the tablet formulations **(Table 2)** were there within the permitted ranges. Drug's accuracy statistics **(Table 3)** revealed a high percentage recovery and percentage RSD, with values ranging from 99.4 to 101.3 and 0.2 to 0.4. The values of intra & inter-day precision **(Table 4)** were obtained to be 0.79 & 0.57 respectively.

Table 1: Optical characteristics and precision of the proposed method

Parameters	Value
Correlation coefficient (r)	0.9998
Beer's law limit (µg/ml)	10-60µg/ml
Absorption Maxima	294 nm
Slope (m)	0.04319
Regression equation (Y= mX+c)	Y= 0.043x-0.002
LOQ (µg/ ml)	4.64
LOD (µg/ ml)	1.54
Intercept (c)	0.00259
Standard Deviation	0.0075

Table 2: Assay of LGPTN tablets

Dosage forms	Label claims (mg)	Amounts found *±SD
Trajenta	5	5.04±0.0722
Linanext	5	4.93±0.056

Table 3: Accuracy data of the drug

Sample ID	Concentration (µg/ml)		(%) Recovery*± S.D	RSD (%)
	Pure drug	Formulation		
80%	40	50	101.4±0.309	0.306
100%	50	50	99.5±0.398	0.41
120%	60	50	99.8±0.221	0.221

Table 4: Precision of the LGPTN working standards

Assay of LGPTN as % of the labeled amount		
Sample No.	**Analyst–I (Intra-day precision)**	**Analyst–II (Inter-day precision)**
1	100.32	
2	101.32	101.52
3	99.88	100.36
4	100.22	101.24
5	99.98	99.87
Mean	100.34	100.54
%RSD	0.57	0.79

Conclusion

This suggested strategy to estimating LGPTN was straightforward, reliable & highly responsive, with high precision as well as accuracy. This approach is designed specifically for evaluating commercialized formulations free of excipients and other additives.

Conflict of Interest

The researchers assert that, they are not having any opposing viewpoints.

Acknowledgement

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