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# Comprehensive Review on Analytical Profile of Antidiabetic Drug



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## ABSTRACT

Glipizide has a place with the class of medications known as sulfonylureas. It brings down glucose by causing the arrival of your body's characteristic insulin. It is utilized to control glucose levels in patients with type 2 diabetes mellitus. Controlling high glucose forestalls kidney harm, visual deficiency, nerve issues, loss of appendages, and sexual capacity issues. The present review assesses the various approaches for analysis of Glipizide in bulk drug as well as various formulations. A concise review represents the compilation and discussion of about more than 34 analytical methods which include HPLC, HPTLC, UPLC, LC-MS, and UV-Spectrophotometry methods implemented for investigation of Glipizide in natural networks, mass examples and in various measurement details. This detailed review will be of great help to the researcher who is working on Glipizide.



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## ABBREVIATIONS

GLP: Glipizide

Log P: Partition co-efficient

HPLC: High-performance liquid chromatography

RP-HPLC: Reverse phase-high performance liquid chromatography

HPTLC: High-performance thin-layer chromatography

UPLC-MS: Ultra-performance liquid chromatography-mass spectrometry

LC-MS: Liquid chromatography-mass spectrometry

TLC: Thin layer chromatography

ICH: International conference on harmonization

SIM: Stability indicating method



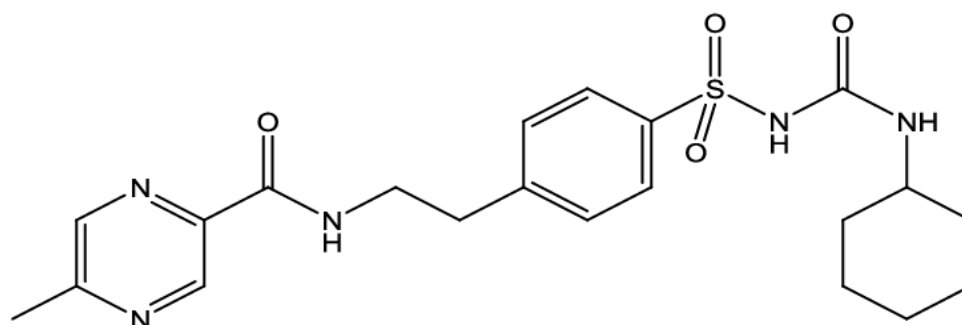
## INTRODUCTION

Diabetes mellitus is a heterogeneous gathering of scatters described by variations from the norm in starch, protein, and lipid digestion. For some patients with Type 2 diabetes, monotherapy with an oral antidiabetic specialist isn't adequate to arrive at target glycaemic objectives and different medications might be important to keep up successful control. Medications having a place with classes, for example, sulfonylureas (for example glipizide, glibenclamide, glimepiride) and thiazolidinedione (TZD) subordinates (pioglitazone, rosiglitazone) are the regularly endorsed hypoglycemic medications for the treatment of non-insulin subordinate sort II diabetes mellitus.<sup>[1]</sup>

Glipizide (GLP) is a medium to long-acting anti-diabetic drug and generally used to bring down the blood glucose level in patients with type two diabetes mellitus. Chemically, Glipizide (GLP) is a substituted aryl-sulphonylurea. As GLP is second era sulfonylurea, which implies it experiences entero-hepatic circulation and act by stimulating the release of insulin from the pancreases and thus decreasing blood glucose level in individuals. GLP ties to  $K_{ATP}$  channels on the cell layer of pancreatic  $\beta$  cells of the islets of Langerhans. This

promptly expanded combination of insulin granular with the cell film and consequently expanded discharge of insulin.

GLP is a practically water-insoluble and poor water-soluble drug but, its supreme bioavailability is near 1 and its disintegration is viewed as rate restricting advance (i.e., a viable factor) in its assimilation from gastrointestinal tract 6, 7. GLP face issue of low bioavailability.<sup>[2]</sup>



**Figure No. 1: Chemical structure of Glipizide**

GLP is given in low dosages. Regarding pharmacokinetic and metabolic examinations of glipizide, a delicate and particular strategy for the assurance of plasma and urine levels of the medication is required.<sup>[3]</sup> Glipizide comes as tablets and extended-release tablets to take by mouth. The regular tablet is usually taken one or more times a day, 30 minutes before breakfast or meals.<sup>[4]</sup> Glipizide, regularly regulated in the portions of 2.5, 5, 10, and 20 mg, has an A1(absorbance 1%, 1 cm at frequency 275 nm) of 237.<sup>[5]</sup>

GLP is administered once every day to manage the postprandial blood glucose level. It is retained after oral organization with basically no first-pass biotransformation of the medication. The peak plasma levels are accomplished inside 1 to 3 hours and the terminal half-lives have been accounted for to extend from 2.4 to 7 hours.<sup>[6]</sup> The human dose of the medications was 2 mg for rosiglitazone and glimepiride, 5 mg for glipizide and glibenclamide, and 1530 mg for pioglitazone. These medications were seen as more than 98-99% bound to plasma protein with a half existence of around 2-7 h after a single oral dose aside from glibenclamide which was widely bound to serum proteins and had a half existence of 10 h<sup>[1]</sup>. Glipizide and Glimepiride eliminate via metabolism by cytochrome P450 (CYP) 2C9 from urine or feces.<sup>[7]</sup>

Self-nano emulsifying drug-delivery systems (SNEDDS) have developed as a powerful delivery framework because of their demonstrated capacity to upgrade the bioavailability of lipophilic drugs. SNEDDS is a thermodynamically steady isotropic blend of oil, surfactant, co-surfactant, and drug that structure an unconstrained oil-in-water nanoemulsion with a bead size less than 100 nm when brought into a fluid medium under delicate fomentation. A few potential focal points of SNEDDS incorporate their capacity to introduce the drug in a solubilized structure inside the gastrointestinal (GI) lumen, subsequently giving more prominent interfacial territory to drug retention, giving more prominent synthetic and enzymatic strength, hindering P-glycoprotein (p-gp) interceded drug efflux, upgrading the lymphatic vehicle. A strong SNEEDS of glipizide by deliberately upgrading the SNEDDS preconcentrate that would create a nanoemulsion on weakening. The age of a nanoemulsion could give an enormous interfacial surface region for tranquilizing solubilization prompting an upgraded dissolvability and disintegration of glipizide. [8] Attributable to its restorative significance various strategies are accessible for assurance of GLP in body liquids and incorporate, HPLC, LC-MS/MS, UPLC-MS/MS and radioimmunoassay. European Pharmacopeia depicts a titrimetric measure in which sedate in dimethylformamide is titrated with lithium methoxide utilizing quinaldine red as a pointer. Strategies dependent on various methods have been recommended for the assurance of GLP in pharmaceuticals including, UV-spectrophotometry, UPLC, TLC, HPTLC, and voltammetry. [9]

**Table No. 1: Drug Profile of Glipizide:**

Drug Name	Glipizide
Category	Oral Hypoglycemic Agent
Chemical formula	C <sub>21</sub> H <sub>27</sub> N <sub>5</sub> O <sub>4</sub> S
IUPAC Name	N-(4-[N-(cyclohexylcarbonyl) sulfamoyl] phenethy)-5 methylpyrazine-2-carboxamide
Molecular weight	445.536 g/mol
Melting point	208 to 209 °C (406 to 408 °F)
Solubility	Insoluble in water and alcohols, but soluble in 0.1 N NaOH; it is freely soluble in dimethylformamide.
BCS Class	Class-II (Low solubility and high permeability)
Half-life	2 to 4 hours
pKa value	5.9
log P value	Log P1.91
CAS No.	29094-61-9

**Glipizide side effects:**

Common Glipizide side effects may include:

- Diarrhea
- Constipation
- Nausea
- Vomiting
- Upset stomach
- loss of appetite
- Headache
- Weight gain
- Skin changes (skin rash, hives, redness, itching, and blisters)

**Serious side effects:**

- Intense hunger
- Nervousness
- Sweating, chills, and clamminess
- Fast heart rate
- Confusion
- Blurred vision
- Depression



**Analytical techniques used for the determination of Glipizide:**

**A. High-performance liquid chromatography (HPLC):**

HPLC is an impelled fluid chromatography used in segregating the join mix of particles experienced in substance and natural structure. In the year 1980, the HPLC system start for the first time looks at mass meds materials (USP,1980). The fundamental bits of HPLC is a dissolvable (A) Pump (B) Injector (C) Segment (D) Detector/Recorder. Every portion is related in a course of action to each other by steel tubing. The pump controls the movement of dissolvable through the framework. After leaving the pump, dissolvable enters the injector, by then experiences the area, in conclusion through the optical unit of a finder. A standard molecule size for column chromatography is 60 microns, while that for HPLC is normally 5 microns, or the size of a spot of buildup dissolvable course through such thick material requires a high weight, so in HPLC the stationary stage is full in a solidified steel chamber, and dissolvable is pumped through the structure under high weight, as much as two or three thousand pounds for each square inch. It extensively uses detectors in HPLC is UV-detectors is prepared to assess a couple of wavelengths is possible to apply the different frequency in inspecting program. UV-locator surety all the UV-draw in parts are distinguished. <sup>[10]</sup> HPLC framework (Waters, USA) comprising of the quaternary pump (Water TM 600), 7725i rheodyne manual injector, and PDA locator and engage II programming were utilized for investigation. <sup>[11]</sup>

**Table No. 2: HPLC method for Glipizide**

Sr. no.	Drug	Method	Stationary phase	Mobile phase	Detection	Linearity, LOD, LOQ (µg/mL)	Rt / Fr	Ref
1	Glipizide, Metformin hydrochloride	RP-HPLC	Cosmosil C-18 (250 mm × 4.6 ID, particle size-5 micron).	methanol and water (60:40) v/v; pH adjusted to 3 with OPA)	226 nm	Linearity: 1-5µg/mL Glipizide LOD: -0.055 µg/mL LOQ: -- 0.167 µg/mL Metformin hydrochloride LOD: - 1.68 µg/ml LOQ: - 5.09 µg/mL	Glipizide Rt: 5.571 min Fr: 0.8 mL/min Metformin hydrochloride Rt: 4.159 min	12

2	Glipizide	RP-HPLC UV	C18 column (ZORBAX ODS 4.6 × 150 mm)	0.01 M potassium dihydrogen phosphate and acetonitrile (65:35, v/v) adjusted to pH 4.25 with glacial acetic acid	275 nm	Linearity: 50-1600 µg/mL LOD: - LOQ: -50 µg/mL	Fr: 1.5 mL/min	13
3	Glipizide, tolbutamide	HPLC	Spherisorb ODS (C <sub>18</sub> ) reversed-phase column (250 mm x 4.5 mm I.D.; 5 µm particle size)	Mixture of acetonitrile-0.01 M phosphate buffer pH 3.5 (35:65)	275 nm	Linearity: 0-1000 µg/mL LOD: - LOQ: -	Glipizide Rt: 10.5 min Fr: 1.5mL/min Tolbutamide Rt: 8.2 min Fr: 1.5 mL/min	3
4	Glipizide Glibenclamide and Glimeperide	RP-HPLC	microbondapak C-18 column, 300mm×3.9mm	mixture of 0.03 molar TBAHS in water adjusted the pH to 6.0 with 1N sodium hydroxide and acetonitrile (50:50v/v)	225 nm	Linearity: 100-300 µg/mL LOD: -0.06 µg/mL LOQ: -0.1 µg/mL Glibenclamide LOD: -0.08 µg/mL LOQ: -0.12 µg/mL Glimeperide LOD: -0.08 µg/mL LOQ: -0.12 µg/mL	Rt: Fr: 1.0 mL/min	14
5	Glipizide	RP-HPLC	Inertsil ODS 3V (150 × 4.6mm; 5µm particle size)	10mM potassium dihydrogen phosphate (pH 3.9) and methanol (60:40)	220nm	Linearity: 1-450 µg/mL LOD: -0.03 µg/mL LOQ: -0.09 µg/mL	Rt: <10min Fr: 1 mL/min	9

				v/v)				
6	Glipizide, Metformin Hydrochloride	RP-HPLC	Symmetry C18 (4.6 × 150 mm, 5 μm, Make: Thermosil)	methanol: phosphate buffer pH 4.5 (65:35)	225 nm	Linearity: 100 - 500 μg/mL Glipizide LOD: - 2.94 μg/mL LOQ: - 9.94 μg/mL Metformin HCl LOD: - 2.96 μg/mL LOQ: - 9.96 μg/mL	Glipizide Rt: 3.78 min Metformin HCl Rt: 2.55 min Fr: 0.8 mL/min	15
7	Glipizide	RP-HPLC	Thermo Hypersil – Keystone; Hy Purity, C18 stainless steel column [5μ, 15cm x 4.6mm]	methanol: 0.115% w/v of ammonium dihydrogen phosphate in water with pH adjusted to 6.0 with 2M of sodium hydroxide [(45:55) v/v]	225nm	Linearity: 10 to 70 μg/mL LOD: - 2 μg/mL LOQ: -10 μg/mL	Rt: 12.724 Fr: 1 mL/min	16
8	Glipizide, Metformin HCl AND Repaglinide	RP-HPLC	Zodiac C18, 150mm x 4.6mm, 3.5μ	buffer (1.0gm of Potassium dihydrogen phosphate in 1000mL, pH 3.0 with diluted orthophosphoric acid	210 nm	Linearity: 10-60 μg/mL LOD: - LOQ: -	Glipizide Rt:3.7min Metformin HCl Rt:1.4min Repaglinide Rt:9.8min Fr: 1.0 mL/min	4
9	Glipizide,	HPLC	Bondclone C18	10mM potassium	225nm	Linearity: 15-800 μg/mL	Rt: 11.5 and 8.6 min	6



			column (10mm, 300×3.9m m	phosphate monobasic and methanol (40:60 [vol=vol], pH 3.5)		LOD: - LOQ: - 15 µg/mL	Fr: 1.0mL/min	
10	Glipizide, Gliclazide , Glibenclamide, Glimepiride, Gliquidone, Repaglinide	RP- HPLC	Alltima C18 column (5 m, 150 mm × 4.6 mm)	methanol– phosphate buffer (pH 3.0; 0.01 mol/L) (70:30, v/v)	228nm	Linearity: 1, 5, 10, 20, 50, 80, 100 µg/mL LOD: -3:1 µg/mL LOQ: -10:1 µg/mL	Rt: Fr: 1.0 mL/min	17

### B. UV- visible spectrophotometric method:

UV-visible spectroscopy is examining the wavelength of a typical sample. The UV-visible spectra have expensive highlights that are restricted use for test identification are helpful for quantitative estimations. The spectrophotometric method is most significant technique is recognize the substance element on-premise of transmission or reflection properties of the material as the capacity of wavelength, adheres to the Beer-Lambert's law and a synthetic compound which bear a chromophoric bunch for retention of light, it consumes the less time when contrasted with other technique and gives incredible accuracy in practical.<sup>[10]</sup> Derivative spectrophotometric techniques, distinction spectrophotometry, and bichromatic strategies can likewise be applied for end of foundation retention as well as dispersing, however, every one of these techniques is pretty much unpredictable. Additionally, derivative spectrophotometry brings about a progressively complex range.<sup>[18]</sup>

**Table No. 3: UV- Spectrometric Method for Glipizide**

Sr. No.	Drug	Method	Solvent	Detection	Linearity LOD, LOQ	Ref.
1	Glipizide, Metformin HCl	SHIMADZU double beam UV/Visible Spectrophotometer model UV 1800s	water	Glipizide: 232nm Metformin HCl: 272nm	Linearity Glipizide 20-50 µg/mL Metformin HCl 5-25 µg/mL Glipizide LOD:0.608 µg/mL LOQ 1.854 µg/mL Metformin HCl LOD:0.214 µg/mL LOQ:0.649µg/mL	19
2	Glipizide	JASCO double beam UV/Visible spectrophotometer (Model V-530)	Methanol	274nm	Linearity 5-25 µg/mL LOD: LOQ:	20
3	Glipizide	Shimadzu Pharmspec UV 1800 ultraviolet-visible spectrophotometer	phosphate buffer pH 7.4 ± 0.1	230 nm, 225 nm, and 235 nm,	Linearity 1-20 µg/mL LOD: 0.27 µg/mL LOQ: 0.82 µg/mL	18
4	Glipizide, Metformin	double-beam UV-Visible spectrophotometer, 1700 pharma sec	Methanol	Glipizide: 276nm Metformin:237nm	Linearity 2-20 µg/mL LOD: LOQ:	21
5	Glipizide	UV-Vis spectrophotometer 1700, Make: Shimadzu	0.1N NaOH	276 nm	Linearity 10-30 µg/mL LOD: 0.542 µg/mL LOQ: 1.643 µg/mL	22
6	Glipizide	Shimadzu Pharmaspec 1700UV/Visible double beam spectrophotometer	0.1M NaOH or 0.1M HCl	0.1M NaOH at 260nm or in 0.1M HCl at 255nm	Linearity 4 -72 µg/mL NaOH Method LOD:1.020 µg/mL LOQ: 3.05 µg/mL HCl Method LOD: 0.85 µg/mL LOQ:2.55µg mL	23
7	Glipizide	UV-VIS Spectrophotometer	0.1N NaOH	227 nm	Linearity 10-50 µg/mL LOD: 0.52 µg/mL LOQ: 0.61µg/mL	24

**C. High-performance thin-layer chromatography (HPTLC):**

High-Performance Thin Layer Chromatography (HPTLC) is the most impressive propelled type of Thin Layer Chromatography (TLC) and comprises of chromatographic layers of most

extreme partition productivity and the use of complex instrumentation for all means in the strategy incorporate exact example application, normalized reproducible chromatogram improvement and programming controlled assessment. HPTLC is an idea that incorporates a generally normalized strategy dependent on logical realities just as the utilization of approved strategies for subjective and quantitative investigation. HPTLC meets all quality necessities for the present systematic labs, to build the goals, and to permit progressively precise quantitative estimations. HPTLC is the most exceptional type of present-day TLC. It employs HPTLC plates including little particles with a restricted size dispersion which brings about homogenous layers with a smooth surface to be obtained. [25]

HPTLC is a most adaptable strategy and is known for consistency, immaculateness profile, measure and exactness, and precision of results. It can deal with a few examples of even dissimilar nature and structure. Most labs use TLC/HPTLC for examination, test, or assessment with practically identical models, screening of indistinct models, or an enormous number of tests. Quality control, sensible R&D, process watching, and biological labs find TLC/HPTLC as an important instrument for standard examination. [10]

**Table No. 4: HPTLC Method for Glipizide:**

Sr. No.	Drug and Matrix	Stationary phase	Mobile phase	Chamber saturation/ TLC plate development time	Detection	Linearity, LOD, LOQ (µg/mL)	Ref.
1	Glipizide, Metformin	precoated silica gel 60F254 TLC plates (10×10cm)	water: methanol: 0.5% w/v ammonium sulfate solution 6:3:1.5 (v/v/v)	Glipizide Rf: 0.85±0.01	236nm.	Linearity 50 -250 µg/mL R <sup>2</sup> :0.9930 LOD:9.57 µg/mL LOQ:29.01µg/mL	26
2	Glipizide	precoated silica gel 60F254 plates with 0.2 mm layers of silica gel	toluene: methanol (8:2; v/v)	Rf: 0.35± 0.02	230nm	Linearity 100- 700 µg/mL R <sup>2</sup> : 0.9992 LOD: 3:1 µg/mL LOQ: 10:1 µg/mL	27

#### D. Stability indicating method:

A Stability-indicating assay method can be characterized as “Approved quantitative expository method that can distinguish the change with time in the chemical, physical or microbiological properties of the medication substance and medication items are explicit so the substance of dynamic fixings and corruption items can be precisely estimated without obstruction”. [28]

The chemical stability of pharmaceutical molecules involves incredible worry as it influences the wellbeing and adequacy of the medication item. The FDA and ICH directions express the necessity of stability testing information to see how the nature of a medication substance and medication item changes with time affected by different natural variables. Information on the stability of particle helps in choosing appropriate definition and bundle just as giving legitimate stockpiling conditions, what's more, the timeframe of realistic usability, which is basic for administrative documentation. Forced degradation is a procedure that includes degradation of medication items and tranquilizes substances at conditions more extreme than quickened conditions what's more, in this manner creates degradation items that can be concentrated to decide the stability of the particle. The ICH rule expresses that stress testing is proposed to recognize the presumable degradation items which further aids in the assurance of the natural stability of the atom and setting up degradation pathways and to approve the stability-indicating procedures utilized. It has become compulsory to perform stability studies of new drug moiety before filing in the registration dossier. The stability studies include long term studies (12 months) and accelerated stability studies (6 months). But intermediate studies (6 months) can be performed at conditions milder than that used in accelerated studies. [29]

These ICH guidelines are relevant to forced degradation study:

- ICH Q1 A: Stability testing of new drug substances and products.
- ICH Q1 B: Photostability testing of new drug substances and products.
- ICH Q2 B: Validation of analytical procedure, methodology. [10]

Forced Degradation Studies of Glipizide in Bulk and Pharmaceutical Dosage Form Following methods were performed for forced degradation studies:

- Acid hydrolysis (using HCl)
- Alkali hydrolysis (using NaOH)
- Oxidation (using H<sub>2</sub>O<sub>2</sub>)
- Photolysis (under sunlight)
- Thermal method (in a hot oven).<sup>[30]</sup>

**Table No. 5: Stability indicating method for Glipizide**

Sr. No.	Method	Drug	R.T&R. T of Degradation Product/Development Time Rf value of drug	Column/ Stationary phase	Mobile Phase & Flow Rate, Chamber saturation time	Wavelength, Linearity, Coefficient correlation.	LOQ & LOD (µg/mL)	Ref
1	HPLC	Glipizide	Run time- Retention time -4.02min	Alltima CN column (250 mm 4.6 mm 5µ)	ammonium formate buffer (pH 3.5) and acetonitrile at a ratio of (45:55, v/v).	227 nm Linearity 1.25–150 µg/mL R <sup>2</sup> : - 0.9999	LOD: 0.796 µg/mL LOQ: 2.412 µg/mL	31
2	RP-HPLC	Glipizide	Run time: Retention time:	phenomenex C18 column (150 × 4.6 mm, i.d., 5 µm)	0.05% Triethylamine (pH-3.5, adjusted with ortho phosphoric acid), acetonitrile and methanol in the ratio of 55:15:30	248nm Linearity 0.1, 1, 5, 10, 20, 50, 100 µg/mL R <sup>2</sup> : -0.9990 ± 0.0004.	LOD: LOQ:	1

3	HPLC-UV	Glipizide	Run time:27min Retention time: (<4%)	XTerra® C18 column (250 × 4.5 mm id)	buffer (0.005 M KH <sub>2</sub> PO <sub>4</sub> ; pH 3.0)–methanol (60 + 40, v/v; mobile phase A) and (20 + 80, v/v; mobile phase B	230nm Linearity 0.2–100, 0.1–100, 0.5–100, 0.2–100, and 0.1–50 µg/mL R <sup>2</sup> :	LOD: 0.07, 0.05, 0.16, 0.08, and 0.05 µg/mL LOQ: 0.20, 0.14, 0.50, 0.23, and 0.14 µg/mL	32
4	LC	Glipizide	Run time: Retention time:	C18 Supelco analytical column (250 mm × 4.6 mm, 5	of 2 mM sodium dodecyl sulphate, acetonitrile (37.5%) and potassium dihydrogenphosphate (62.5%)	225nm	LOD:4. µg/mL LOQ:7.5 µg/mL	33
5	LC-MS/MS	Glipizide	Run time:15min Retention time:	Zorbax Extend-C18 column (100 mm × 3.0 mm i.d., 1.8 µm;	mobile phase A consisted of 0.1% formic acid in acetonitrile, and the mobile phase B consisted of 0.1% formic acid in water	Linearity 10–1000, 40–4000, 10–1000, 10–1000, and 2–200 µg/mL R <sup>2</sup> : 0.9978	LOD: LOQ:	34
6	RP-HPLC	Glipizide	Run time: 5.3 min Retention time:	Phenomenex Luna C18 column (250 mm × 4.6 mm id, 5 µm)	Acetonitrile: Water, 0.2% triethylamine(pH 3.0 adjusted with ortho-phosphoric acid) (60:40 v/v)	258 nm Linearity 1-5 µg/mL R <sup>2</sup> : 0.9987	LOD: 0.113 µg/mL LOQ: 0.34 µg/mL	30
7	TLC	Glipizide	Run time: Retention time:	precoated TLC silica gel 60 F254 plates (Macbrey-NaGel	Chloroform methanol (90:10 v/v)	276nm Linearity 280-800 µg/mL	LOD: LOQ:	35

### E. Bio-analytical method:

These bioanalytical validation techniques built up by Karnes et al. in 1991 which was deliberate to guide bioanalytical scientific experts. Following one year, Shah et al. set up

these reports the show on Analytical technique validation of bioavailability, bioequivalence, and pharmacokinetic contemplates composed in Washington in 1990. <sup>[10]</sup>For the last 15–20 years, method validation has been the subject of numerous conversations. A general direction on bioanalytical method validation was given at the 1990 AAPS/FDA workshop. In 2000, new workshops tended to the validation of bioanalytical methods just as the unique instance of tests committed to macromolecules. In 2001, the United States Food and Drug Administration (FDA) distributed its notable direction report on bioanalytical method validation. <sup>[36]</sup>

It is likewise critical to underscore that each bioanalytical technique has its qualities, which will differ from analyte to analyte. In these cases, explicit approval rules may be created for each analyte. Also, the propriety of the technique may likewise be affected by a definitive goal of the investigation. At the point when test examination for a given report is led at more than one site, it is important to approve the bioanalytical method(s) at each site and give proper approval data for various locales to set up interlaboratory unwavering quality.

The procedure by which a particular bioanalytical strategy is created, approved, and utilized in routine example examination can be isolated into:

1. reference standard preparation,
2. bioanalytical method development and establishment of assay procedure and
3. application of the validated bioanalytical method to routine drug analysis and acceptance criteria for the analytical run and/or batch. <sup>[37]</sup>

Table No. 6: Bioanalytical method for Glipizide

Sr. No.	Method	Drug	Bio. Fluid	Column	Mobile Phase	Flow Rate & Retention Time	Detection /Detector	Linearity & LOD& LOQ	Ref
1	UPLC-MS-MS	Glipizide	Human plasma	Acquity BEH C18 column (2.1 mm 3 50 mm, 1.7 mm)	acetonitrile and water (containing 0.1% formic acid).	Flow rate: 0.4 mL/min Retention time: 0.62min	-	Linearity 10–1,500 µg/mL  LOD:  LOQ:	38
2	HPLC-UV	Glipizide, Indapamide	Human plasma	Inertsil ODS-3 analytical column (25 cm × 4.6 mm i.d., 5µm	5% buffer solution (2 g KH <sub>2</sub> PO <sub>4</sub> , 3 ml H <sub>3</sub> PO <sub>4</sub> and 3.5 ml triethylamine in 1 l of H <sub>2</sub> O), 40% acetonitrile and 5% methanol for 12.5 min, and then a gradient flush from 100% isocratic to a mixture of 20% isocratic mobile phase and 80% methanol for 3 min.	Flow rate: 1.0 mL/min Retention time: Glipizide 12.3 min Indapamide 10.3 min	UV detector 240 nm	Linearity Indapamide 10–400 µg/mL  LOD: 10 µg/mL  LOQ:	39
3	LC/MS/MS	Glipizide	Rat plasma	C18-column (50 x 4.6mm, 5µm)	0.01% (v/v) formic acid and methanol in 1:9(v/v)	Flow rate: 0.5 mL/min Retention time: 1.56min	-	Linearity 50,100, 250,500, 1000,2500,5000 and 10000 µg/mL  LOD: 25 µg/mL  LOQ: 50 µg/mL	40
4	LC-MS/MS	Glipizide	Monkey plasma	Thermo Fluophase PFP- reverse phase column (50 mm × 2.1 mm; 5m particle	40% of 0.1%FA in ACN and 60% of 10 mM ammonium formate solution	Flow rate:0.6 mL/min Retention time: 0.8min	-	Linearity  LLQ: 98.7 -101%  ULQ: 92.1–103%	41



				size)					
5	RP-UPLC	Glipizide	Human plasma	Acquity UPLC BEH C18 (50 mm × 2.1 mm, 1.7 μm) column	0.001 M sodium dihydrogen phosphate with pH-6.0 buffer and methanol in ratio of 55:45	Flow rate:0.3 mL/min. Retention time:	276 nm UV detector.	Linearty 0.55 -16 μg/mL LOD: LOQ:	42
6	RP-HPLC	Glipizide	Guinea pig plasma	PC-Micra NPS RP18, (length × OD × ID =33 × 8.0 × 4.6 mm, 1.5 μm)	Phosphate Buffer (pH 3.5), acetonitrile, and THF in 80:15:5	Flow rate:0.4 mL/min Retention time: 2.01 min	275 nm UV detector	Linearity 1, 3 and 5μg/mL LOD: 6.45 μg/mL LOQ: 18.6 μg/mL	43
7	LC	Glipizide	Human Serum	Nucleosil, C18 (10 μm, 25 9 0.46 cm)	80:20 methanol: water with pH adjusted to 3.5	Flow rate: 1 mL/min Retention time: 3.13min	230nm UV detector	Linearity 0.15–5 μg/mL LOD: 20 μg/mL LOQ: 70 μg/mL	7
8	LC-MS/MS	Glipizide	Human plasma	Aglient Zorbax SB-Phenyl, 150 × 2.1 mm 5μm	acetonitrile: water (50:50) with 10 mM ammonium acetate and 0.02% TFA (50:50, v/v)	Flow rate: 0.3 mL/min Retention time:	-	Linearity 1–2000 μg/mL LOD: LOQ:	

## SUMMARY

The present review illustrates various analytical approaches exercised for the estimation of Glipizide. A numerous investigation had performed including, Bio-analytical, Stability indicating, HPLC, HPTLC, UV-Visible Spectroscopy, and LC-MS, etc. for estimation of Glipizide in bulk and its combined pharmaceutical formulations and in plasma. while hyphenated such as UPLC, LC-MS, RP-HPLC detection methods are reported for determination of Glipizide and its metabolite in plasma and other biological fluids. Few chromatography approaches like HPTLC and UV Spectrophotometry methods are also used for the assay of Glipizide.

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