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ESTIMATION OF GLIBENCLAMIDE IN PHARMACEUTICALS - A REVIEW

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ABSTRACT

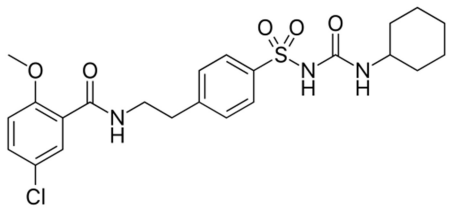
Glibenclamide belongs to the class second generation sulfonyl ureas used in the management of diabetes. The present review is generalized to describe the various methods of UV, HPLC, HPTLC, UPLC and UHPLC for glibenclamide analysis in formulations, synthetic mixtures and biological fluids. The chromatographic conditions used for the analysis were performed under various experimental conditions and combinations. Analytical parameters such as wavelength, solvent, mobile phase, correlation coefficient, linearity, retention time, retardation factor, LOD, LOQ and so on are written in this review. For budding researchers, this review is very helpful in the analysis of glibenclamide in formulation, biological fluids and synthetic mixtures.

Keywords: Glibenclamide, Metformin Hydrochloride, Pioglitazone, Glimepiride, HPLC, chromatography, flow rate, retention time

INTRODUCTION

Type 2 diabetes mellitus (DM) is a chronic metabolic prevalence disorder which results in becoming an epidemic in some of the countries, the affected people to double in next decade **[1]**. Glibenclamide is 5-chloro-N-[2-[4-(cyclohexyl carbamoyl sulfamoyl) phenyl] ethyl]-2-methoxybenzamide, with molecular weight 494 g/mol **[2]**. As of 2003, it was most popular sulfonyl urea in the United States **[14]**. Glibenclamide is used in

treatment of NIDDM (non-insulin dependent diabetes mellitus. It is a long acting, effective, second generation sulfonyl urea. At pH 4 the solubility of it is approximately 4 µg/ml, 600 µg/ml at pH 9 and in alcohol 3 mg/ml. Its pKa is 6.8. Glibenclamide shows its action on functional beta cells of pancreas and stimulate release of insulin thereby decreasing blood glucose level. After extended administration, hypoglycemic effects appear connected to extra pancreatic effects like increase peripheral sensitivity to the insulin, depletion in production of basal hepatic glucose, then later may result in changes in the events following to insulin binding or increase in insulin receptor number **[3]**.



Glibenclamide

METHODS FOR ESTIMATION

UV Spectrophotometric methods:

Various UV Spectrophotometric methods for estimation of Glibenclamide single and combination with other drugs are developed and are listed in the **(Table 1)**.

Chromatographic methods:

Various chromatographic methods like HPLC, HPTLC, ion chromatography GC, UPLC, UHPLC, was developed for estimation of Glibenclamide in single and combination with other drugs. Methods for estimation of HPLC, HPTLC, UPLC and UHPLC are listed in the **(Table 2-5)**.

Table 1: Methods for estimation of Glibenclamide single and combination with other drugs by UV Spectrophotometry

S. No.	Drugs	Application	Description	Reference
1.	Glibenclamide	In bulk and pharmaceutical dosage form	Detection wavelength: 229 nm Solvent: Acetonitrile:0.2M Sodium hydroxide solution(20:80) v/v Linearity range: 5-3 µg/ml Correlation coefficient: 0.999	[4]
2.	Glibenclamide	In bulk and pharmaceutical formulation	Detection wavelength: 308 nm Solvent: Methanol: Water(50:50) v/v Linearity range: 10-70 µg/ml Correlation coefficient: 0.9998	[5]
3.	Glibenclamide (Glyburide)	In bulk and pharmaceutical dosage form	Detection wavelength: 242 nm Solvent: Chloroform Linearity range: 5-30 µg/ml Correlation coefficient: 0.9934	[6]
4.	Glibenclamide	In bulk and pharmaceutical formulation	Detection wavelength: 230 nm Solvent: Ethanol: Water(1:5) v/v Linearity range: 2-14 µg/ml Correlation coefficient: 0.995	[7]
5.	Saxagliptin Hydrochloride and Glibenclamide	In synthetic mixture	Detection wavelength: Saxagliptin Hydrochloride: 229 nm Glibenclamide: 315 nm	[8]

			Solvent: Methanol Linearity range: Saxagliptin Hydrochloride: 5-25µg/ml Glibenclamide: 5-25 µg/ml Correlation coefficient: Saxagliptin Hydrochloride: 0.9995 Glibenclamide: 0.9994	
6.	**Glibenclamide**	**In pure and tablet dosage form**	**Method A: Detection wavelength: 276 nm Solvent: Water and Ethanol Linearity range: 1-5 µg/ml Correlation coefficient: 0.9967 Method B: Reagent: MBTH MBTH:3-methyl 2-benzothiazoline hydrazone Detection wavelength: 630 nm Solvent: Water and Ethanol Linearity range: 1-5 µg/ml Correlation coefficient: 0.9773**	**[9]**
7.	**Metformin Hydrochloride and Glibenclamide (Glyburide)**	**In combined tablet dosage form**	**Detection wavelength: Metformin Hydrochloride: 233 nm Glyburide:301 nm Solvent: Methanol, Acetonitrile and Water Linearity range: Metformin Hydrochloride: 8-12 ppm Glyburide: 80-120 ppm Correlation coefficient: Metformin Hydrochloride: 0.9994 Glyburide: 0.998**	**[10]**
8.	**Metformin hydrochloride and Glibenclamide**	**In bulk drug and pharmaceutical dosage form**	**METHOD I Detection wavelength: Metformin hydrochloride: 237 nm Glibenclamide: 229.2 nm Solvent: Methanol Linearity range: Metformin hydrochloride: 2-10 µg/ml Glibenclamide: 2-14 µg/ml Correlation coefficient: Metformin hydrochloride: 0.9998 Glibenclamide: 0.9999 METHOD II Detection wavelength: Metformin hydrochloride: 237 nm Glibenclamide: 225 nm Solvent: Linearity range: Metformin hydrochloride: 2-10 µg/ml Glibenclamide: 2-14 µg/ml Correlation coefficient: Metformin hydrochloride: 0.9998 Glibenclamide: 0.9984**	**[11]**
9.	**Glibenclamide and Metformin Hydrochloride**	**In bulk drug and pharmaceutical formulation**	**Detection wavelength: Glibenclamide: 300 nm Metformin Hydrochloride: 233 nm Solvent:0.1N Hydrochloric acid solution Linearity range: Glibenclamide: 10-60 µg/ml Metformin Hydrochloride: 2-12 µg/ml Correlation coefficient: Glibenclamide: 0.9988 Metformin Hydrochloride: 0.999**	**[12]**

Table 2: Methods for estimation of Glibenclamide single and combination with other drugs by HPLC

S. No.	Drugs	Application	Description	Reference
10.	Metformin and Glibenclamide	In bulk and tablet dosage form	Detection wavelength: 228 nm Mobile phase: Methanol: Acetonitrile: Water(30:60:10) v/v/v Column: Oyster-BDS RP-C18 Flow rate: 1 ml/min Linearity range: Metformin: 200-450 µg/ml Glibenclamide: 2-4.5 µg/ml Retention time: Metformin: 3.17 min Glibenclamide: 8.10 min	[13]
11.	Glibenclamide, Metformin Hydrochloride, Rosiglitazone maleate	In tablet dosage form	Detection wavelength: 238 nm Mobile phase: Methanol:20 mM Potassium dihydrogen phosphate buffer(78:22) v/v Column: C18 Flow rate: 1 ml/min Linearity range: Metformin Hydrochloride: 50-250 µg/ml Rosiglitazone maleate: 0.4-2.0 µg/ml Glibenclamide: 0.6-3.0 µg/ml Retention time: Metformin Hydrochloride: 2.51 min Rosiglitazone maleate: 3.90 min Glibenclamide: 8.12 min	[14]
12.	Metformin Hydrochloride and Glibenclamide	In combined tablet dosage form	Detection wavelength: 220 nm Mobile phase: Acetonitrile: Mono basic sodium phosphate buffer(50:50) v/v Column: Agilent Hypersil ODS Flow rate: 1 ml/min Linearity range: Metformin Hydrochloride:125-450 µg/ml Glibenclamide: 0.25-2.0 µg/ml Retention time: Metformin Hydrochloride: 2.709 min Glibenclamide: 9.216 min	[15]
13.	Glibenclamide	In rat serum	Detection wavelength: 253 nm Mobile phase: Acetonitrile:25mM monobasic potassium dihydrogen orthophosphate(60:40) v/v Column: C_{18} Linearity range: 0.1-10 µg/ml Mean recovery: 97.12%	[16]
14.	Glibenclamide	In tablet dosage form	Detection wavelength: 233 nm Mobile phase: Potassium dihydrogen phosphate buffer: Acetonitrile(60:40) v/v Column: Chromosil Flow rate: 1 ml/min Linearity range: 10-50 µg/ml Retention time: 6.2 min	[17]
15.	Metformin, Pioglitazone and Glibenclamide	In tablet dosage form	Detection wavelength: 230 nm Mobile phase: Acetonitrile:Water:0.5% Potassium dihydrogen phosphate(60:20:20) v/v/v Column: Phenomenex luna CN Flow rate: 1 ml/min Linearity range: Metformin: 50-300 µg/ml Pioglitazone: 1.5-9.0 µg/ml Glibenclamide: 0.5-3.0 µg/ml Retention time: Metformin: 2.2 min Pioglitazone: 2.8 min	[18]

			Glibenclamide: 5.8 min	
16.	Glibenclamide	In human serum	Detection wavelength: 253 nm Mobile phase: Acetonitrile:25 mM Phosphate buffer(3:2) v/v Column: C_{18} Analytical column Flow rate: 1 ml/min Linearity range: 50-500 ng/ml Mean recovery rate: 92%	[19]
17.	Metformin and Glibenclamide	In combined tablet dosage form	Detection wavelength: 256 nm Mobile phase: Methanol: Acetate buffer(75:25) v/v Column: Develosil ODS HG-5 RP C18 Flow rate: 1 ml/min Linearity range: Metformin: 2-10 µg/ml Glibenclamide: 3-15 µg/ml Retention time: Metformin: 2.24 min Glibenclamide: 3.28 min	[20]
18.	Glibenclamide	In nano emulsion formulation	Detection wavelength: 228 nm Mobile phase: Methanol:0.2 M Phosphate buffer(70:30) v/v Column: Gemini 5µ C18 110A Flow rate: 1 ml/min Linearity range: 1-2 µg/ml Retention time: 3.2 min	[21]
19.	Pioglitazone Hydrochloride, Metformin Hydrochloride and Glibenclamide	In multicomponent tablet dosage form	Detection wavelength: 227 nm Mobile phase: Acetonitrile: Methanol: Water(70:10:20) v/v/v Column: Agilent TC-C18 Flow rate: 1ml/min Linearity range: Pioglitazone Hydrochloride: 5-30 µg/ml Metformin Hydrochloride: 5-30 µg/ml Glibenclamide: 2-10 µg/ml Retention time: Pioglitazone Hydrochloride: 6.82 min Metformin Hydrochloride: 2.42 min Glibenclamide: 9.40 min	[22]
20.	Metformin Hydrochloride , Pioglitazone Hydrochloride and Glibenclamide	Three component tablet dosage form	Detection wavelength: 230 nm Mobile phase: Acetonitrile: Potassium dihydrogen phosphate buffer(60:40) v/v Column: C18 Flow rate: 1.2 ml/min Linearity range: Metformin Hydrochloride: 200-1000 ng/ml Pioglitazone Hydrochloride: 200-1000 ng/ml Glibenclamide: 200-1000 ng/ml Retention time: Metformin Hydrochloride: 1.75 min Pioglitazone Hydrochloride: 2.22 min Glibenclamide: 6.483 min	[23]
21.	Glibenclamide and Atenolol	In bulk	Detection wavelength: 235 nm Mobile phase: 0.01N Potassium dihydrogen orthophosphate: Acetonitrile(55:45) v/v Column: BDS C18 Flow rate: 1 ml/min Linearity range: Glibenclamide: 2.5-15 µg/ml Atenolol: 6.25-37.5 µg/ml Retention time: Glibenclamide: 2.322 min	[24]

			Atenolol: 3.260 min	
22.	Metformin, Pioglitazone, Sitagliptine, Repaglinide, Glibenclamide and Gliclazide	Application for counterfeit analysis	Detection wavelength: 220 nm Mobile phase: (Gradient) Acetonitrile:0.05MPotassium dihydrogen phosphate:0.01M Sodium octane sulphonate Column: Kromosil 100-C18 Flow rate: 0.85 ml/min Linearity range: Metformin: 0.05-205 µg/ml Pioglitazone: 0.05-100 µg/ml Sitagliptine: 0.05-100 µg/ml Repaglinide: 0.1-100 µg/ml Glibenclamide: 0.05-100 µg/ml Gliclazide: 1-100 µg/ml Retention time: Metformin: 2.24 min Sitagliptine: 3.13 min Pioglitazone: 6.3 min Gliclazide: 7.41 min Glibenclamide: 8.41 min Repaglinide: 14.32 min	[25]
23.	Six anti diabetic drugs including Glibenclamide	In pharmaceutical drug products	Detection wavelength: 210 nm Mobile phase: Phosphate buffer: Acetonitrile Column: C18 Flow rate: 0.6 ml/min Linearity range: Metformin Hydrochloride: 10-60 µg/ml Pioglitazone: 10-60 µg/ml Glipizide: 10-60 µg/ml Gliclazide: 10-60 µg/ml Glibenclamide: 10-60 µg/ml Glimepiride: 10-60 µg/ml Retention time: Metformin Hydrochloride: 2.2 min Pioglitazone: 7.5 min Glipizide: 11.4 min Gliclazide: 14.5 min Glibenclamide: 16.7 min Glimepiride: 17.9 min	[26]

Table 3: Methods for estimation of Glibenclamide single and combination with other drugs by HPTLC

S. No.	Drug	Application	Description	Reference
24.	Metformin Hydrochloride and Glibenclamide	In combined dosage form	Detection wavelength: Metformin Hydrochloride: 232 nm Glibenclamide: 238 nm Mobile phase: Methanol:Water:0.4% Sodium sulphate in water(7:5:11) Stationary phase: Aluminium coated with silica Gel 60 F254 Linearity range: Metformin Hydrochloride: 250-1750 ng/spot Glibenclamide: 250-1750 ng/spot Retardation factor: Metformin Hydrochloride: 0.27 Glibenclamide: 0.80	[27]
25.	Glibenclamide, Rosiglitazone maleate and Metformin Hydrochloride	In multi component dosage form	Detection wavelength: Glibenclamide: 237 nm Rosiglitazone maleate: 324 nm Mobile phase: Methanol: Tetrahydrofuran: Water: Glacial acetic acid Stationary phase: Precoated RP-18 F254S	[28]

			Aluminium sheets Linearity range: Glibenclamide: 200-1000 ng/band Rosiglitazone maleate: 200-1000 ng/band Metformin Hydrochloride: 120-600 ng/band Retardation factor: Glibenclamide: 0.54 Rosiglitazone maleate: 0.62 Metformin Hydrochloride: 0.80	
26.	Glibenclamide	In tablets	Detection wavelength: 229 nm Mobile phase: Toluene: Ethyl acetate: Methanol(8:0.5:1) v/v/v Stationary phase: Silica Gel 60 F254 Linearity range: 40-200 ng/band Retardation factor: 0.45±0.07	[29]

Table 4: Methods for estimation of Glibenclamide single and combination with other drugs by UPLC

S. No.	Drug	Application	Description	Reference
27.	Chlorpropamide, Glipizide, Tolbutamide, Pioglitazone, Gliclazide, Glibenclamide, Glimepiride	In pharmaceutical dosage form	Detection wavelength: 245 nm Mobile phase: Buffer (5 mM ammonium acetate pH 4.0 adjusted with formic acid) and B: a mixture of 90% acetonitrile and 10% buffer (gradient) Column: Acquity UPLC BEH C18 (50mm × 2.1 mm, 1.7 µm) (Waters, Ireland) column Flow rate: 0.613 ml/min Linearity: Chlorpropamide: 500-7550 µg/ml Glipizide: 10-150 µg/ml Tolbutamide: 1000-15000 µg/ml Pioglitazone: 30-450 µg/ml Gliclazide: 160-2400 µg/ml Glibenclamide: 5-75 µg/ml Glimepiride: 4-60 µg/ml Retention time: Chlorpropamide: 0.64 min Glipizide: 0.70 min Tolbutamide: 0.76 min Pioglitazone: 0.88 min Gliclazide: 0.94 min Glibenclamide: 1.11 min Glimepiride: 1.19 min	[30]
28.	Glibenclamide	In oral dosage form	Wavelength: 272 nm Mobile phase: Methanol and Acetonitrile in the ratio of (80:20)v/v Column: Hypersil C18 (100 mm x 2.1 mm, 1.7 µm) Flow rate: 1.2 ml/min Linearity: 2-10 µg/ml Retention time: 8.623±0.11 min	[31]

Table 5: Methods for estimation of Glibenclamide single and combination with other drugs by UHPLC

S. No.	Drug	Application	Description	Reference
29.	Glipizide, Gliclazide, Glibenclamide, Glimepiride, Gliquidone, Repaglinide	Analysis of counterfeit anti diabetic drugs	Instrument: Agilent 1220 Infinity Gradient LC system Detector: DAD(Diode Array Detector) Wavelength: 230 nm/16 nm Ref.: off Mobile phase: Methanol:10 mM phosphate buffer, pH 3 (65:35) Column: Agilent ZORBAX RRHD Eclipse Plus	[32]

			C18, 3 × 50 mm, 1.8 µm (p/n 959757-302) LOD: Glipizide: 38 pg, Gliclazide: 46 pg, Glibenclamide: 44 pg, Glimepiride: 80 pg Gliquidone: 67 pg, Repaglinide: 214 pg LOQ: Glipizide: 127 pg, Gliclazide: 153 pg Glibenclamide: 148 pg, Glimepiride: 268 pg, Gliquidone: 222 pg, Repaglinide: 714 pg	
30.	**Vildagliptin, Alogliptin, Sitagliptin Phosphate Hydrate, Linagliptine, Mitiglinide Calcium Hydrate, Glibenclamide and Glimepiride.**	**In combination tablets**	**Wavelength: UV 220 nm Detector: PDA detector HITACHI L-2455U Eluent: a)10mM HCOONH4/ CH3CN/HCOOH (900/100/1), b) CH3CN/HCOOH (1000/1) gradient mode Column: HITACHI LaChromUltra C18, 50 mm x 2.0 mm I.D, 2 µm Flow rate: 0.6 ml/min Auto sampler: HITACHI L-2200U Data system software: HITACHI EZChrom Elite**	**[33]**
31.	**Glibenclamide**	**In glibenclamide related substance**	**Wavelength: 230 nm Mobile phase: A) 20:50:930 101.8g/L Triethylamine solution/ACN/H2O B): 20:65:915 mobile phase A/H2O/ACN Column: Kinetex® 2.6 µm C18 100 Å, LC Column 100 x 4.6 mm, Ea Flow rate: 0.8ml/min Retention time: Glibenclamide impurity A: 1.827 min Glibenclamide impurity B: 2.205 min Glibenclamide: 3.063 min Gliclazide: 4.112 min**	**[34]**

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CONCLUSION

A broad range of analytical techniques are available in estimation of Glibenclamide in bulk drug and in different pharmaceutical dosage forms. From the analysis of documented data out of all these techniques HPLC with UV detection was extensively used with mobile phases Methanol, Acetonitrile, Toluene, Ethyl acetate, Sodium octane sulphonate and Potassium dihydrogen phosphate. Flow rate of 0.6-1.2 ml\min and retention time less than 10 min because this approach offers reliable and low cost in comparison with more advanced technology. This article provides a summary of the Glibenclamide literature, in particular the analytical and formulation-related data referred to in **Table 1 - 5**. This tabulated data would undoubtedly be useful for all researchers currently working on Glibenclamide research projects.

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