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QUANTIFICATION OF GLICLAZIDE TABLETS AND THEIR FORMULATIONS: HPLC AND UV- SPECTROPHOTOMETRY METHODS

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Abstract:

A UV spectrophotometry and RP-HPLC method for the Gliclazide tablets quantification in the developed method is described. Both the methods were validated according to ICH Q2 R (1) guidelines for linearity, accuracy, precision, the limit of detection, the limit of quantification, specificity, and robustness. HPLC was run in isocratic mode on a reversed-phase C18 column (250×4.6 mm internal diameter and particle size of 5 µm) ACN: Water: TEA: TFA (50:50:0.1:0.1) as the mobile phase maintaining a flow rate of 1.0 ml/min. Gliclazide drug showed an absorbance maximum (λmax) in methanol 228 nm and 7.4 pH phosphate buffer solution 226 nm which was used for the UV spectrophotometry determinations. The calibration curve of the Gliclazide drug showed linearity in the required concentration range (R2>0.999) by both the UV and HPLC methods. Both the methods were found to be precise and accurate with a recovery range of 98–101% and a relative standard deviation <2%. Most importantly, the accuracy and precision achieved by the HPLC method, correlated closely with the UV method. The current study also involves the detection and quantification of Gliclazide drug released from its formulations by both the developed methods. This paper demonstrates the high correlation (R2≥0.98) between the UV and HPLC methods when determining the release of the Gliclazide drug from various formulations. With this established correlation, we hereby suggest that, for routine analysis, UV spectrophotometry can be an economic, simple, reliable, and less time-consuming alternative to expensive and time-consuming Chromatographic analysis.

Keywords: *Gliclazide drug, UV spectrophotometry, High-Performance Liquid Chromatography method, Validation study*

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INTRODUCTION:

Gliclazide drug (GLA) (Fig 1.) is a moderate molecular weight is (323.411 g/mol), Gliclazide is an oral hypoglycemic drug useful for the treatment of non-insulin-dependent diabetes mellitus (type 2 NIDDM) and Gliclazide is eventually, second-generation sulfonylurea which binds to a specific sulfonylurea receptor on the pancreatic β-cells to enhance insulin secretions in the body. Based on the literature, the Gliclazide drug is poorly soluble in water (42.6 µg/ml) and highly soluble in chloroform, slightly dissolve in methanol or ethanol. In all vertebrates, Serum albumin is the most important protein in the blood. The tertiary structure of albumin is highly conserved across species and composed of three largely helical domains because the bovine serum albumin (BSA) shows highly similar to human serum albumin (HSA). Mechanism of drug molecule and albumin are very important in the pharmacological study, because of determining the free drug concentration and its bio-availability, and the pharmacokinetics process in the body. Gliclazide is acted by stimulating β cells of the pancreas to release insulin, and recently the anti-glycation effect of this drug on in vitro AGE formation was demonstrated. A single oral dose of Gliclazide tablets, 40 to 120 mg drug results in a maximum plasma concentration of 2.2 to 8.0 µg/mL within 2 to 8 hr. The protein binding affinity of Gliclazide is from 85 to 97%, and this ligand is bound mainly to site II of the HSA molecule, located in subdomain IIIA, with the involvement of the aromatic ring of 411Tyr. Gliclazide drug is poorly soluble in water (42.6 µg/ml) on the basis that its dissolution varies 1) in the small intestine and stomach where it has a different degree of solubility 2) with extensive metabolism in the liver, and 3) with physiological and formulation characteristics. Currently, Gliclazide formulation does not provide patient compliance since 2-3 tablets per day are required to meet the daily therapeutic dose due to its poor solubility and bio-availability. Current research indicated that the formulation aimed to enhance the dissolution of Gliclazide can increase its absorption in GI. Evaluated the effect of mixing hydrophilic polymers on the release profile of Gliclazide from a tablet using hydrophilic polymers HPC GF, HPMC K 4M, and PARTICK ® SR P-80 polymers which are known for their potential to prolong the release of the drug. In addition, HPC GF has a low water affinity and hence hydrates slowly preventing lumping during the preparation of the sample. HPMC K4M (hypromellose) is a highly viscous polymer and thermally gel. Hypromellose provides the release of a drug in a controlled manner and effectively increases the release profile of a drug and prolongs its therapeutic effect. Parteck® SR P-80 is a new functional polymer based on polyvinyl alcohol (PVA) and it has posed a matrix diffusion mechanism that helps to increase bio-availability. Parteck® SR P-80 is highly compatible with the direct compression technique. This is aimed to develop Gliclazide tablet in such a way that a single dose can provide the required daily therapeutic dose, thereby increasing patient compliance and reducing the cost of the treatment by reducing cost per dose as well as the number of doses.

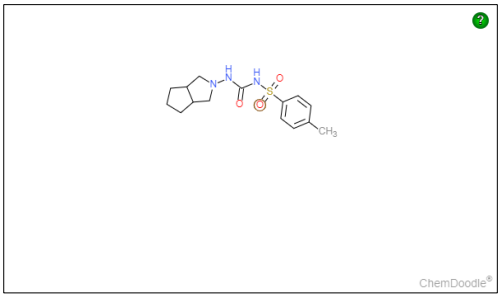


Fig.1 Structure of Gliclazide drug

To determine the content of the Gliclazide drug and its release from the formulation with different hydrophilic polymers, UV-Spectrophotometry, and high-performance liquid chromatography is necessary to have a simple, specific, fast, and validated analytical method. But these methods include a more extensive sample preparation process and long Chromatographic runs which involve a certain set of conditions to be maintained. Mobile phases containing certain compounds such as Triethyl-amine (TEA) and Trifluoroacetic (TFA) acid, Acetonitrile, etc, may affect the column life span. Modified HPLC methods are developed in this work which uses simple solvents such as mobile phase water, Acetonitrile, Triethyl-amine (TEA), and Trifluoroacetic (TFA) (50:50:0.1:0.1v/v). Eventually, the simplicity of the validated method, HPLC has certain disadvantages such as it being time-consuming. Moreover, a particular level of experts is required for the handling of such complex and sophisticated instruments. Hence, a simple, specific, accurate, precise, and reproducible method of UV-Spectrophotometry for the quick estimation of Gliclazide drug would be highly beneficial for routine analysis of Gliclazide drug. The UV-Spectrophotometry method is an easy and effective method, which provides a quick analysis of the Gliclazide formulations. Currently, there is a lack of information regarding the UV-Spectrophotometry method for the quantitative determination of Gliclazide drugs. Herein, the method developed is one using methanol as a solvent as Gliclazide is

insoluble in water. The developed method was optimized and validated as per the guidelines given by International Conference on Harmonization (ICH) guidelines. This study also demonstrated the linearity, accuracy, and robustness of the proposed method for the determination of Gliclazide drugs prepared with the different hydrophilic polymers. The objective of this study is to correlate the two determination methods; UV-spectrophotometry and HPLC analysis. Based on the established correlation, we propose the use of the UV-spectrophotometry method as a simple method for quantification of the Gliclazide drug.

Table 1. The optimized formulation for the stability study

Sr. No	Ingredients	Batch G1	Batch G2	Batch G3	Batch G4	Batch G5	Batch G6
1	GLICLAZIDE	30	30	30	30	30	30
2	HPC GF	60	-	-	-	-	60
3	AVICEL PH 101	8	-	-	-	-	-
4	HPMC K 4M	-	-	-	-	15	-
5	PARTECK ® SRP80	-	30	60	15	-	-
6	STARCH 1500	-	38	8	53	53	8
7	MG. STEARATE	1	1	1	1	1	1
8	AEROSIL 300	1	1	1	1	1	1
9	TOTAL	100MG	100MG	100MG	100MG	100mg	100MG

MATERIALS AND METHODS:

Materials:

Gliclazide was obtained from Bajaj Healthcare; HPC GF grade polymer was obtained from Ashland (always solving) and used for sustaining the release of the drug; HPMC K4M was obtained from Dow and used as a rate-limiting polymer; Parteck® SRP 80 polymer has obtained from Merck well suited for direct compression processes and accelerates formulation; Avicel pH 101 FMC used as a diluent; Starch 1500 was obtained from Colorcon and; Magnesium stearate was obtained from SD Fine chemical Ltd and used as a lubricant and Aerosil 300 was obtained Evonik and used as Glidant. and Acetonitrile and water employed for the preparation of mobile phases were of HPLC grade (Rankem). All the other chemicals and solvents viz. Triethylamine (TEA) and Trifluoroacetic (TFA) acid are of ambient grade. All other chemicals and reagents used were of analytical grade.

Methods:

Direct Compression Technique:

The instrument was used a Rotary press machine (Eliza press) and round shape punches of 8mm were used and tablet weight was 200 ± 7.5 mg Compressed with 10,30 KN for ejected from the die. Pure drug and diluent and binding agents were passed through 60 mesh sieves and Glidant and lubricant were passed through 30 mesh sieves, to improve the compressibility and flowability of the material. V-cone-shaped blender (Wintech pharmachem equipment Pvt. Ltd.) This was helpful for uniform mixing of the blend and blended for 10 min..

Determination of the wavelength in Methanol and 7.4 pH Phosphate buffer solution.

In the 10 ml volumetric flask, 10 mg of pure Gliclazide drug was weighed accurately and transferred. Approximately, 1ml of the standard stock solution was taken in a 10 ml volumetric flask. It was further diluted using methanol and 7.4 Phosphate buffer solution to give 10 µg/ml of concentration. This solution was scanned via UV Spectrophotometry through the range of 200-800 NM for the determination of the wavelength of maximum absorption by pure Gliclazide drug (λ max).

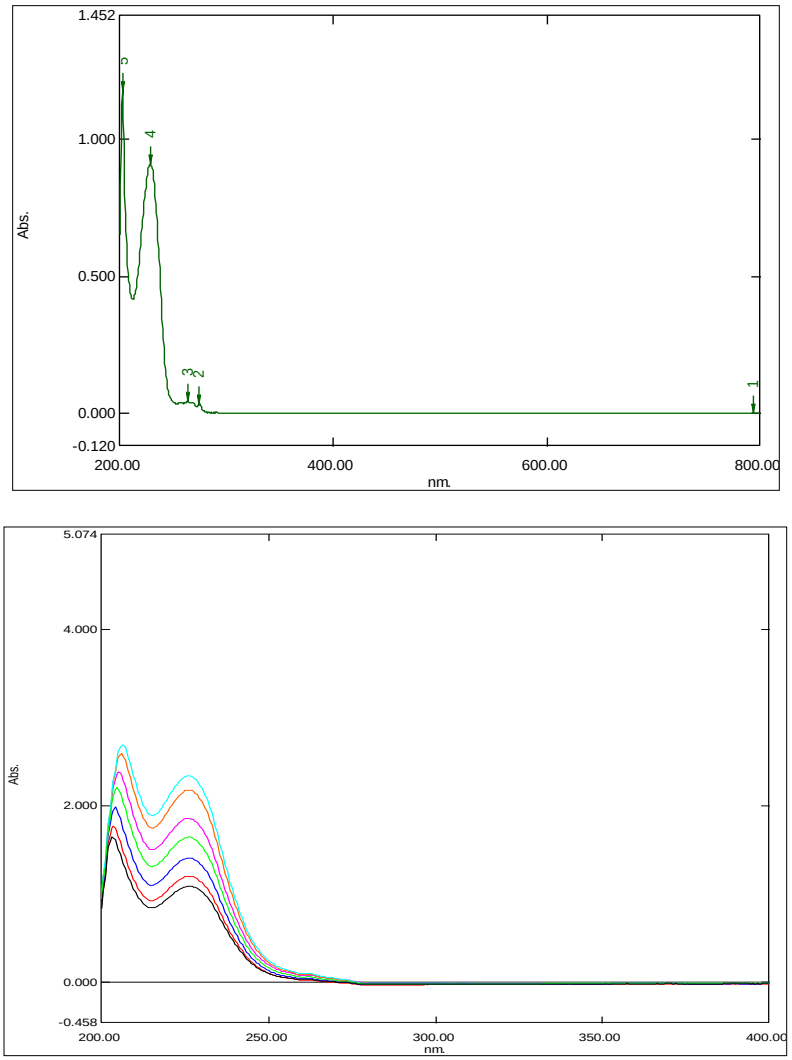


Fig.2, 3 Determination of the wavelength in Methanol and 7.4 pH phosphate buffer solution

Preparation of standard solutions in Methanol:
In the 10 ml volumetric flask, 10 mg of pure Gliclazide drug was weighed accurately and transferred. Methanol was used to make up to the final volume of 10 ml, to make a concentration of 1000 µg/ml. From the above standard solution, 1 ml was transferred to another 10 ml volumetric flask add methanol to make up the level of the 10 ml volumetric flask. A standard stock solution of 100 µg/ml was prepared for the UV Spectrophotometry analysis. From this primary stock solution, working standards of concentration from 2 to 12 µg/ml were prepared for UV Spectrophotometry analysis.

Preparation of standard solutions in 7.4 pH Phosphate buffer solution

In the 10 ml volumetric flask, 10 mg of pure Gliclazide drug was weighed accurately and transferred. 7.4 pH Phosphate buffer was used to make up the final volume of 10 ml, to make a concentration of 1000 µg/ml. From the above standard solution, 1 ml was transferred to another 10 ml volumetric flask add 7.4 pH Phosphate buffer was to make up the level of the 10 ml volumetric flask. A

standard stock solution of 100 µg/ml was prepared for the UV Spectrophotometry analysis. From this primary stock solution, working standards of concentration from 2 to 12 µg/ml were prepared for UV Spectrophotometry analysis.

Preparation of standard solution for HPLC:
Accurately weighed about 10 mg of Gliclazide drug and transferred into a 10ml volumetric flask and 5 ml of Acetonitrile was added and kept in an ultrasonic bath to ensure the complete solubilization and the volume was adjusted with ACN to get the stock solution of 1000 µg/ml. Then appropriate dilutions were made to produce standard solutions with concentrations ranging from 5-100 pp.

Instrumentation and analytical conditions:
High-performance liquid chromatography (HPLC) system equipped with JASCO AS 2055 Plus Intelligent auto-sampler (JASCO Tokyo, Japan) and a JASCO MD-2018 Plus Intelligent HPLC pump. It consists of a Quaternary pump, a photodiode array detector, and a rheodyne injection valve with a 100 µL loop with a web degasser. The chromNAV software program was accustomed calculate all the height areas. The optimum chromatographic conditions were obtained on a synchronic C18,250×4.6 mm and particle size 5 µm column (Thermo-Scientific technologies). The mobile phase composition was water, Acetonitrile, TEA, and TFA (50:50:0.1:0.1v/v). It was filtered through a 0.45 µm nylon filter and sonicated (Enertech fast ultrasonicate cleaner, Mumbai) for 20 min. Wavelength was set at λmax of the Gliclazide drug. The mobile phase was pumped at a rate of 1ml/min with a 20 µl injection volume. All experiments were administered at the temperature of 25±2 °C and performed within the isocratic mode in triplicate also the entire area of drug peak was accustomed to quantifying Gliclazide drug and formulations. These conditions were optimized to supply a straightforward and reliable method with the most effective peak resolution for symmetry, tailing, reduced run time, and lower the worth of research. The chromatographic conditions are tabulated in Table 2. UV spectrometry was dispensed using UV Spectrophotometry (Labman Scientific Instruments, India). Absorbance was measured using a 1 cm quartz cell against a blank sample.

Method validation: System suitability:
System suitability tests were carried out on freshly prepared standard stock solutions of Gliclazide drug and it was calculated by determining the standard deviation of Gliclazide drug standards by injecting standards in six replicates at 6 minutes intervals and the values were recorded. The percent coefficient of variation (%CV) of ≤ 2% for the peak area and retention times for the Gliclazide drug was set as the acceptance.

Linearity*:*
From the standard stock solution, the various dilutions of Gliclazide in the concentration of 1, 5, 10, 15, 20, 30, 40, 50, and 100µg/ml were prepared. The solutions were injected using 20µl injection volume into the Chromatographic system at the flow rate of 1 ml/min and the effluents were monitored at 235 NM, Chromatographic were recorded given in table 2. The calibration curve was obtained by plotting the peak area ratio versus the applied concentrations of Gliclazide. The linear correlation coefficient was found to be 0.999 and is shown in table 2.

Table 2 Chromatographic conditions

Parameters	Method
Stationary Phase (column)	BDS Hypersil (250 x 4.6 mm)
Mobile Phase	ACN: Water: TEA: TFA (50:50:0.1:0.1)
pH	2.04 ±0.05
Flow Rate(ml/min)	1
Run Time(min)	15
Column Temperature (ºC)	Room Temperature
The volume of Injection (µL)	20
Detection Wavelength (nm)	235
Retention Time (min)	11.9

Table 3 Linearity of Gliclazide drug with the help of HPLC and UV method

Linearity of Gliclazide drug (HPLC) method		Linearity of Gliclazide drug (UV-Spectrophotometry) method	
Concentrations(ppm)	**Peak Area**	**Concentration µg/ml**	**Wavelength 226 NM in 7.4 pH phosphate buffer**
1	1183 ± 217.6	2	0.104 ± 0.001
5	5069.667 ± 756.0	4	0.2115 ± 0.0007
10	10118.33 ± 444.1	6	0.304 ± 0.001
15	15117.67 ± 630.2	8	0.4025 ±0.002
20	20055.33 ± 1121.8	10	0.4975 ±0.003
30	30235 ± 123.7	15	0.742 ± 0.002
40	40317.67 ± 902.8	20	0.9945 ± 0.0007
50	51518.33 ± 636.3	Equation	Y = 0.0498x
100	98607.33 ± 4127.7	R^2	R^2 = 0.9996

Intra-day and inter-day precision studies The precision of an analytical method may be defined because of the degree of repeatability under normal operational conditions. The precision of the strategy was applied by determining the repeatability (intra-day) and intermediate precision (inter-day) of the samples and %RSD was reported for replicate measurements. Intra-day was resolute by analyzing the samples thrice each day by UV Spectroscopy and HPLC at different time intervals. Inter-day studies were disbursed by preparing and analyzing the aliquot solutions prepared from different stock solutions on three consecutive days

Limit of detection (LOD) and limit of quantification (LOQ)

The lowest amount of analyte that the analytical method can dependably differentiate from the ground noise levels is termed because of the limit of detection. On the opposite hand, the rock bottom concentration on the linearity curve which may be measured accurately and with precision and variability is termed because of the limit of quantification. The limit of detection and quantification was firm from the quality deviation of the intercept and slope of the calibration curve, as per ICH guidelines Q2 (R1) as shown in Eqs. (1, 2). LOD = 3.3x σ⁄S ….(1)

LOQ = 10xσ⁄S ……(2)

where σ=a variance of y-intercept; S=slope of the calibration plot.

Accuracy and recovery

The accuracy of an analytical procedure was evaluated using a recovery test. The high recoveries with a low % RSD value indicated that the method had good accuracy and specificity. Accuracy was expressed in percentage (observed concentration × 100 / theoretical concentration). % recovery of Gliclazide was within the acceptable limits of 98% and 102%. The results of recovery studies confirm the accuracy of the method.

Robustness:

To determine the robustness of the method, it was run on a different instrument with the same column dimension. Statistical analysis showed no significant difference between results obtained from two different instruments. Thus the method showed to be robust which is shown in the above table 2.

Ruggedness:

Inter-day variations were performed by using six replicate injections of standard and sample solutions of concentrations which were prepared and analyzed on three different days over one week. Ruggedness was also expressed in terms of percentage relative standard deviation and statistical analysis showed no significant difference between results obtained employing the different analysts.

Specificity

Injections of placebo samples were conformed to perform the specificity of the method. An obtained result showed the excipients mixture of tablets shows no specific peak at the RT of analyte peak. A solution

containing the drug a mixture of the tablets excipients was prepared using the sample preparation procedure to evaluate possible interfering peaks. Other components in the solution did not affect the peak and retention time of Gliclazide showing the specificity of the method. The specificity of the method where there is no interference of other substances in the retention time of the analytical peak.

Assay of Gliclazide tablet

Three different batches of Diamicron were analyzed using the validated method. For the analysis, six replicates of every batch were assayed. The tablets were weighed and finely powdered. An accurately weighed portion of the powder, like about 10 mg of Gliclazide was transferred to a 100 ml volumetric flask followed by the addition of 25 ml of Acetonitrile. After sonicating the answer for five minutes, volume was adjusted to urge 100 ppm solution and so filtered through a 0.45 µm filter. The results were presented in table 4. All the analyzed batches presented Gliclazide drug was very near the labeled amount. The content within the tablet samples varied from 99.2 to 100.2%.

Table 4 Assay of Gliclazide Tablets

Sample Tablet	Batch	Content of Gliclazide(%) ±SD
Diamicron	1	99.2±0.25
	2	99.55±0.32
	3	100.2±0.45

Assay of developed formulated Gliclazide tablets

Assay of the prepared formulation of Gliclazide tablets was calculated using both methods. A 10 mg equivalent of powder was weighed from the formulation. Then, 10 µg/ml of Gliclazide drug solution was prepared, and it was quantified according to the UV and HPLC method developed. The experiment was performed in triplicates.

Release study

An In-vitro drug release of Gliclazide tablets was studied by, using dissolution apparatus II paddle (Electrolab Model TDT 08, India) as per the in-house developed method. 900 ml of 7.4 pH Phosphate buffer because the dissolution medium was placed within the dissolution vessels, and also the temperature was maintained at 37 ± 0.5 °C. The rotation speed of the paddle was 75 rpm. At predetermined time intervals (2, 6, 12, 16, and 24 hours), 10 ml of dissolution medium was removed for determining a drug concentration and a fresh medium was replaced. The quantity of Gliclazide released within the dissolution medium was measured employing a UV Spectrophotometry and HPLC method at the wavelength of 226 nm and 235nm.

RESULTS AND DISCUSSION:

Method development

Gliclazide drug shows insoluble in water and is found to be easily soluble in Acetonitrile. In the HPLC, Water, Acetonitrile, TEA, and TFA (50:50:0.1:0.1v/v) were used as a solvent for analysis. The wavelength of maximum absorption after scanning was found to be 235 nm. The chromatogram was obtained for the analyzed standard and sample solution of Gliclazide using the developed method. Gliclazide drug eluted well and showed separation from the solvent front. The retention time of 11.9 min provided a determination.

HPLC system suitability Results of six replicate analyses of 100 µg/ml concentration for the system suitability studies were in an acceptable range. The %RSD was found to be 0.13 and 0.43 for peak area and retention time, respectively as shown in Table 5. Gliclazide drug was repeatedly well eluted at 11.9 min expressing excellent suitability and a good repeatability of replicate sample analysis. Thus, it can be inferred that the developed method is suitable for Gliclazide drug analysis.

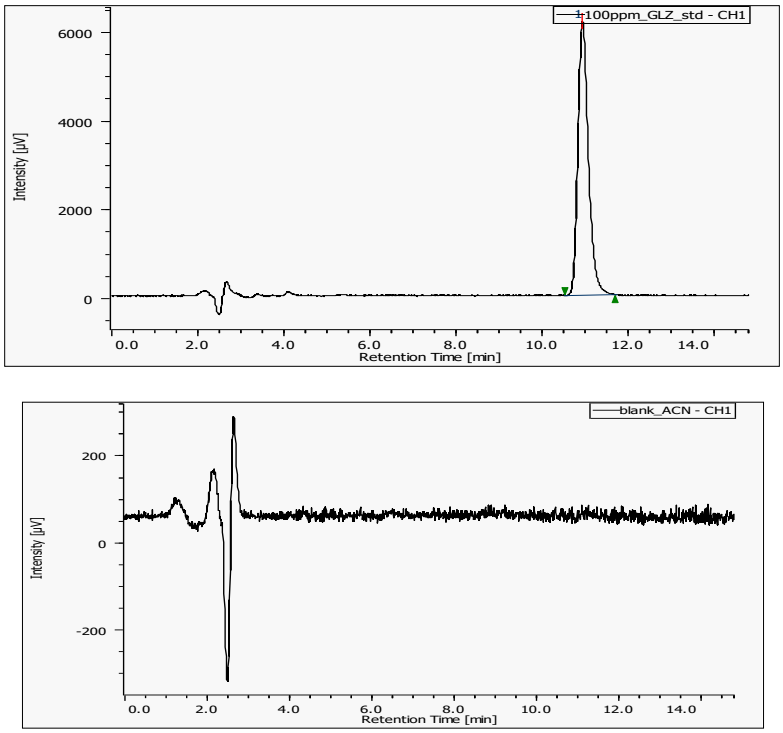


Fig.4,5. Chromatograph of Standard Gliclazide drug in ACN and Placebo Tablets

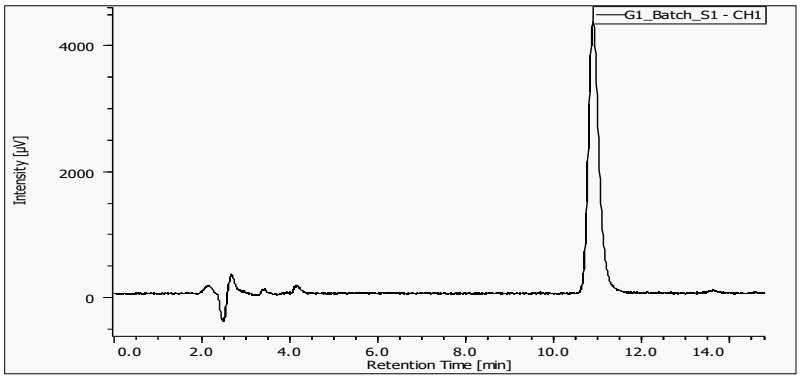


Fig. 6 Chromatograph of formulated tablets

Table 5 System Suitability for Gliclazide

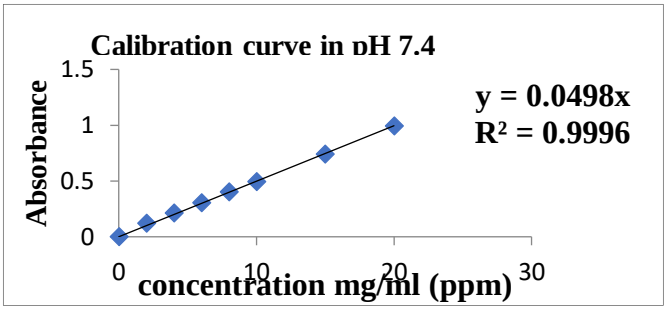
Concentration	Injection	Area	R t
100 ppm	Inj-1	101841	11.975
	Inj-2	102105	11.933
	Inj-3	101921	11.95
	Inj-4	101712	11.95
	Inj-5	102067	12.075
	Inj-6	101964	11.95
Statistical Analysis	Mean	101935	11.9721
	SD	132.8696	0.052136
	%RSD	0.130347	0.435479

Method validation

The UV and HPLC method developed was validated for Linearity, Inter-day, and Intra-day studies, Stability, Accuracy, Recovery, Robustness, Ruggedness, and Specificity in step with the rules set by the International Conference of Harmonization (ICH).

Linearity

The calibration curve showed a good linear relation over the concentration range of 2-12 µg/ml for UV Spectrophotometry and between 1 and 100 µg/ml for HPLC analysis. The linear equation was found to be Y = 0.0498x for UV spectrophotometry while y = 98607.33+ 4127.7 for HPLC.The correlation coefficient was found to be 0.9996 and 0.9996 for UV and HPLC, respectively. The calibration curve is depicted in Fig. 7 and 8 for UV and HPLC respectively, and the results of the linearity study are depicted in Table 3 for UV Spectrophotometry and HPLC.



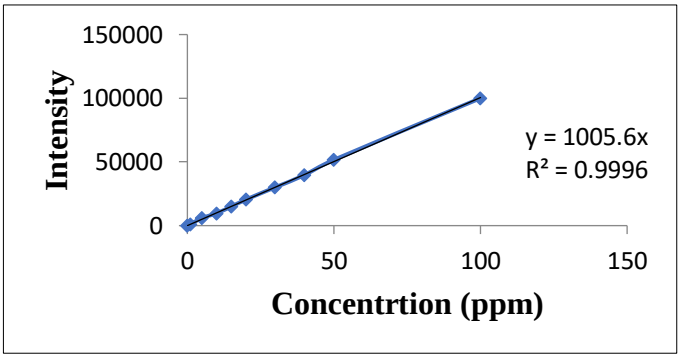


Fig. 7, 8 Linearity curve of 7.4 pH phosphate buffer solution and linearity of Gliclazide drug

Inter-day and Intra-day studies

The results of both intra-day and inter-day studies confirm the high precision and repeatability of the developed methods. All data is expressed in RSD% (≤ 2%). The results of the intra-day and inter-day studies for both, UV and HPLC methods are demonstrated in Table 6. It was found that %RSD for intra-day and inter-day precision studies for the HPLC method and the UV method was within limit respectively.

Table 6 Precision parameter of Gliclazide

Injections	Area
I.P.-1	101841
I.P.-2	102105
I.P.-3	101921
I.P.-4	101712
I.P.-5	102067
I.P.-6	101964
Mean	101935
SD	132.8696
%RSD	0.130347

Accuracy and recovery

The average recovery for each spiked level was been calculated by the peak area of the Gliclazide drug resulting from the solution to that of the standard solution. Both the methods revealed the accuracy with a recovery rate between 99 and 102%. which is found within the limit of detection

Robustness and Ruggedness

The robustness of the HPLC method was established by making deliberate changes within the three parameters. The three parameters viz. mobile phase ratio, flow rate, and also the detection wavelength were varied at 3 levels. The %RSD for all the three parameters in the slightest degree at three levels was found 2%. Thus, it is concluded that the developed HPLC method is strong concerning these three parameters. The information for the robustness of the UV method is specified. At a relentless concentration of 10 µg/ml, the little change within the wavelength range 226 ± 2 nm, did not show any significant change within the absorbance (%RSD = 0.523). This implies that the above method is powerful concerning wavelength. Hence, a small variation within the wavelength does not affect the results. On measuring the absorbance at a continuing wavelength (235 nm) and changing the concentration from 9.8 to 10.2 µg/ml, the % RSD was found to be 0.1303. A small change in concentration drastically affects the absorbance.

Table 7 Ruggedness data of the HPLC method

Parameter	Study condition		Mean area±SD	%RSD of area
	Original	Varied		
Mobile phase ratio (ACN/Water)	70:30	68:32 70:30 72:28	101935±132.8696	0.13
Flow rate (ml/min)	1.0	0.9 1.0 1.1	101712±2318698	0.27
Detection wavelength	235	234 235 236	102035±123.8698	0.12

Table 8 Robustness of the UV method (n=3)

Constant parameter Concentration	Variable parameter Wavelength (NM)	Absorbance	Average Absorbance (Mean±SD)
10 µg/ml	224 225 226 227 228	0.497 0.402 0.449 0.447 0.412	0.441±0.006
Wavelength	**Concentration (µg/ml)**		**(Mean±SD)**
226	9.8 10 10.2	0.517 0.471 0.490	0.492±0.0.245

Specificity

Figure 4,5,6 shows the Chromatographic presentation for the placebo sample, standard, and its SD, justifying that there is no interference of the excipients within the peak of the Gliclazide drug. This ensures the tactic is restricted for the determination of Gliclazide. Similarly, placebo samples were analyzed using the UV method to test the absorbance of the excipients at the λmax of the Gliclazide drug. Interestingly, it was found that the placebo samples showed negligible absorbance at 226 nm and 228 nm, 235 nm as shown in Fig. 4,5, and 6. Hence, the interference must be checked if the formulation is modified. Hence, it may be inferred that the proposed UV and HPLC methods are specific

since no interference was observed with the placebo sample.

Assay of Gliclazide Tablets

The UV and HPLC methods were used to determine the assay of Gliclazide tablets. Results of formulated tablets of Gliclazide showed that content uniformity and an assay of the drug in all samples lies in the range of 95 to 100 % of the %labeled amount with a % RSD of less than 2% No degradation obtained in the products was observed in samples. The formulation was quantified according to the developed methods.

Correlation between the HPLC method and UV method for release data

For the sustained released Gliclazide tablets dissolution media was 7.4 pH phosphate buffer. The percentage release of formulations tablets of Gliclazide drug with the different polymers such as PARTECK® SRP-80, and HPMC K 4M, HPC GF polymers. The G3 formulation showed 14.59 % by UV Spectrophotometry method and 20.28% by HPLC analysis within 2 hr. The G1, G2, G3,G4,G5,G6 percent release within 2 hr. of all formulations of Gliclazide drug with different hydrophilic polymer was 30.85%, 19.10%, 16.86%, 32.98%, 18.67%, 23.19% by UV Spectrophotometry and percent release by HPLC method was obtained 30.87%, 19.125%, 12.04%, 32.98%, 12.80%, and 25.20%. The result revealed that in all the batches, it was observed that as the polymer concentration increased, the drug release rate decreased. This can be attributed to the increase in the thickness of the gel layer thus retarding drug diffusion out of the tablet. Since the diffusion release of the drug Gliclazide may be primarily controlled by the gel thickness (diffusion layer) increasing the polymer concentration tends to decrease the rate of drug release. By using UV Spectrophotometry and Chromatographic methods assay of above formulations was 85.23%, 91.72%, 98%, 96%, 95%, 90.12% etc. The In- vitro drug release profile of prepared different formulations, it was seen that batch G1, G2, G3, G4, G5, and G6 show an initial drug release starting from 18 % in 2 hrs and sustained action for 24 hours with the release of 99 % and considering the Diamicron was marketed tablet as per reference. Formulation G3 (Drug with Parteck SR P-80) was found to be the best formulation because it fulfilled the criteria of the UV method and HPLC methods.

CONCLUSIONS:

The oral route of administration for sustained release drug delivery system plays a measure role to extend the efficiency of the dose, more flexibility, reduced dose frequency, and better patient compliance. Gliclazide, a poorly water-soluble drug may be formulated into SR matrix tablets using HPMC K4M, HPC GF, and Parteck SRP 80 used as release retardant. Formulation of sustained-release drug delivery dosage forms was supported optimization of batches from dissolution profile for stability study and main formulation batches as G1, G2, G3, G4, G5, and G6 within which concentration of polymer of varied grades (HPC GF, HPMC K4M and Parteck SRP 80) varied with the ratio of starch 1500 and Micro-crystalline cellulose. The validation study shows that the developed analytical methods are accurate, rapid, precise, and reproducible with acceptable correlation co-efficient, RSD (%), and standard deviations which make it versatile and valuable for simultaneous determination of Gliclazide from the pharmaceutical dosage form, especially new formulated tablets. The proposed method is easy and does not involve laborious time-consuming sample preparation. The conclusion is that both the methods (UV-spectrophotometry and HPLC) were highly correlated for the Gliclazide quantification from the formulations. Though HPLC is widely used to quantify the Gliclazide, the proposed UV Spectrophotometry method of Gliclazide was found to be simple, economic, quick, accurate, and robust. The low LOD and LOQ values suggest the nice sensitivity of the developed methods. Moreover, the tactic method was sensitive to the concentration of the analyte because it shows a high RSD on deliberately changing the concentration of 10 µg/ml (±0.2 µg/ml), keeping all other parameters constant. The tactic method is robust concerning wavelength within the range of 226 (±2 nm) and 235 nm (±2 nm). The strategy is specified as no other excipients from the placebo, interfering with the analyte of interest. On performing the assay of Gliclazide formulations, the % assay was found to be within the suitable range. The dissolution studies depict the low release of Gliclazide justifying the formation of amorphous Gliclazide tablets. The parity plot shows a high correlation (R2=0.98) within the results given by both methods. Hence, the UV method has been validated and keeping with the results and parameters, it is an appropriate method for fast analysis of Gliclazide in bulk and nutraceutical formulations.

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