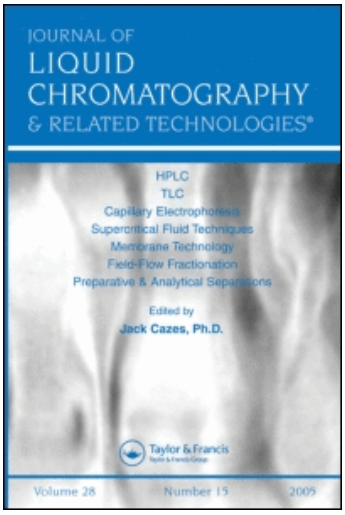

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Quantitation of Glipizide and Glyburide in Tablets Using High Performance Liquid Chromatography

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QUANTITATION OF GLIPIZIDE AND GLYBURIDE IN TABLETS USING HIGH PERFORMANCE LIQUID CHROMATOGRAPHY

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ABSTRACT

Reverse phase high-performance liquid chromatography methods for the quantitation of glipizide and glyburide in tablets have been developed. The methods are accurate and precise with a percent relative standard deviations based on 6 injections of 0.8 and 0.3% for glipizide and glyburide, respectively. The developed methods can be used to test the content uniformity of the tablets. The extraction procedure for the active ingredients from the tablets is very simple. There is no interference from the excipients and the acid hydrolyzed samples showed new peak in the chromatograms.

INTRODUCTION

Both glipizide and glyburide (Figure 1) are antidiabetic drugs and have been extensively used in Europe since long. Recently, these drugs have been approved by the Food & Drug Administration here in USA and are available commercially in the form of tablets.

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In spite of their extensive use, both glipizide and glyburide are not official in the latest USP-NF.

The purpose of these investigations was (i) to develop reverse phase high-performance liquid chromatography methods for the quantitation of glipizide and glyburide in tablets and (ii) to use the methods to test the content uniformity of the tablets.

MATERIALS AND METHODS

Chemicals and Reagents - All the chemicals and reagents were either USP-NF or ACS quality and used without further purification. The powders of glipizide (1) and glyburide (2) were used as received.

Column - A semipolar column (3), 30 cm x 3.9 mm i.d. was used.

Apparatus - The HPLC (4), equipped with a multiple wavelength detector (5) and a recorder (6) was used.

Chromatographic Conditions - The mobile phase contained 24% V/V of acetonitrile (30% V/V for glyburide) in 0.02 M aqueous solution of ammonium acetate. The flow rate was 2.0 ml/min (3.0 ml for glyburide) and the sensitivity was 0.04 AUFS. The detector was set at 232 nm and the chart speed was 30.5 cm/hr. The temperature was ambient.

Stock Solutions - The following stock solutions in methanol were prepared using a simple solution method:

(i) A 0.05% solution each of glipizide and glyburide.

(ii) A 0.063% solution of hydrocortisone (the internal standard).

The standard solutions of glipizide and glyburide were prepared as needed by diluting the stock solutions with 50% methanol solution

in water. Before bringing to volume, an appropriate quantity of the hydrocortisone stock solution was added (final concentration was always 26.0 µg/ml). The most commonly used standard solutions contained 25 µg/ml of glipizide and 50 µg/ml of glyburide. The solutions of other concentrations were prepared as needed.

Assay Solutions from the Tablets - Ten tablets (one if content uniformity was to be tested) were ground to a fine powder. A quantity of the powder representing 2.5 mg of the drug was mixed with 50 ml of methanol (25 ml for glyburide) and 4.0 ml (2.0 ml for glyburide) of the stock solution of hydrocortisone. The mixture was shaken occasionally for 5 minutes and brought to volume (100.0 ml for glipizide and 50.0 ml for glyburide) with water. After mixing, it was filtered (7), the first 10-15 ml filtrate was rejected and then collected for assay.

Assay Procedure - A 20.0 µl quantity of the assay solution was injected into the chromatograph using the described conditions. For comparison, an identical volume of the standard solution was injected after the assay sample eluted. The standard solution contained the same concentrations of the drug and the internal standard based on the label claim as of the assay solution.

Calculations - Since preliminary investigations indicated that the ratio of the peak heights (drug/internal standard) were directly related to concentrations of the drug, the results were calculated using the standard curve or the following equation:

$$\frac{Ph_{ra}}{Ph_{rs}} \times 100 = \text{Percent of the label claim found}$$

where Ph_{ra} is the ratio of the peak heights of the assay solution and Ph_{rs} that of the standard solution. The peak heights versus concentrations were linear between 0.2 to 1.0 µg of glipizide and 0.6 to 1.4 µg of glyburide. The results of these investigations were determined using the above equation.

Decomposed Solutions - A 5.0 ml quantity of the stock solution of either glipizide or glyburide was mixed with either ∿1 ml of ∿1 N NaOH solution or ∿1 ml of ∿1N H_2SO_4 solution. The solution was stored overnight, 20 ml of water added and heated to boiling on a hot plate for ∿30 minutes. More water was added as needed. The mixture was cooled to room temperature and ∿1 ml of ∿1 N NaOH solution was added to the mixture decomposed with sulfuric acid and vice versa. The pH of the solutions were ∿2.6 (± 1) as measured with a pHmeter (8). Fifty ml of methanol (25 ml for glyburide solutions) was added and the mixtures were stored at room temperature for 3 days. A 4.0 ml quantity of the stock solution of hydrocortisone (2.0 ml for glyburide solutions) was added, the mixtures brought to volume (100.0 ml for glipizide and 50.0 ml for glyburide) with water and assayed. Preliminary investigations indicated that there was no interference from the product(s) of decomposition with the hydrocortisone peak.

RESULTS AND DISCUSSION

The results (Table 1) indicate that both glipizide and glyburide can be assayed using the developed methods. The methods are precise and accurate with a percent relative standard deviations based on 6 injections of 0.8 and 0.3 for glipizide and glyburide, respectively. The ratio of peak heights of drug/internal standard were linear

TABLE 1
Assay Results

Tablets of	Claim mg/tab	Color	Percent of the Claim Found
Glipizide	5.0	white	100.8
Glipizide[a]	5.0	white	100.2
Glipizide	10.0	white	99.4
Glipizede[a]	10.0	white	99.8
Glyburide	2.5	pink	100.3
Glyburide[a]	2.5	pink	100.0
Glyburide	5.0	green	99.8
Glyburide[a]	5.0	green	100.3

RECOVERY DATA

Synthetic Mixtures

5.0 mg of glipizide and 250 mg of lactose	99.8%
10.0 mg of glipizide and 250 mg of lactose	100.0%
1.25 mg of glyburide and 150 mg of lactose	100.2%
2.5 mg of glyburide and 150 mg of lactose	100.%

[a]Different lot.

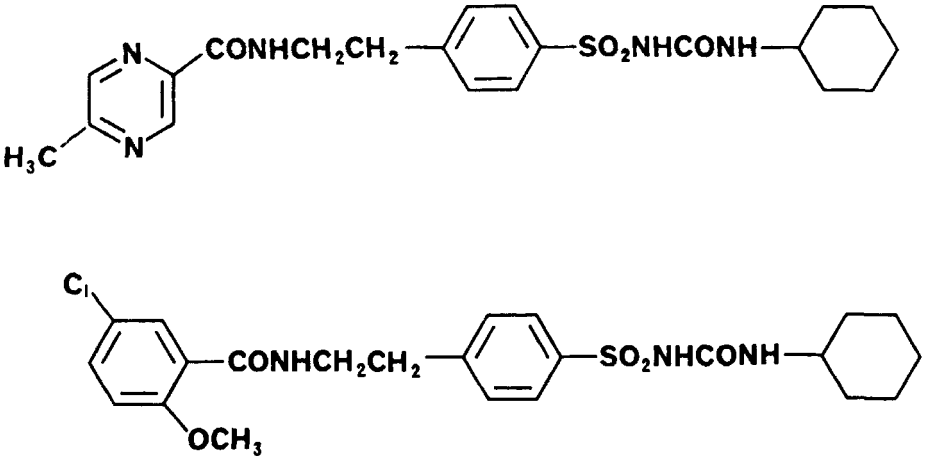

Figure 1 - Structures of glipizide (upper) and glyburide (lower).

TABLE 2
Content Uniformity Results

	Glipizide 5 mg Tablets		Glyburide 2.5 mg Tablets	
Tablet Number	Weight (mg)	Percent of the Claim Found	Weight (mg)	Percent of the Claim Found
1	201.7	100.7	221.8	97.6
2	198.0	98.7	226.4	102.4
3	198.9	99.3	225.3	101.7
4	200.4	100.0	220.8	98.2
5	202.0	101.3	223.9	100.3
6	201.0	101.0	221.2	99.1
7	202.6	101.3	226.0	102.0
8	201.0	100.0	223.9	99.7
9	201.3	100.0	220.6	98.3
10	199.3	98.2	221.8	98.9
Averages	200.6	100.1	223.2	98.8

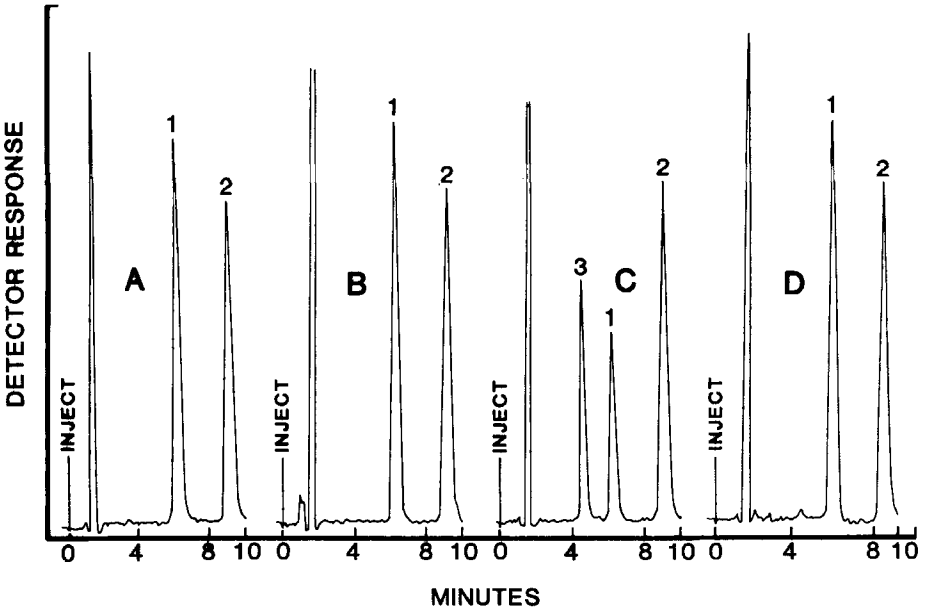

Figure 2 - Sample chromatograms. Peaks 1-3 are from glipizide, hydrocortisone (the internal standard) and the decomposition product, respectively. Chromatogram A is from a standard solution; B from 5 mg tablets; C from a solution decomposed with sulfuric acid and D from a solution decomposed with sodium hydroxide. For chromatographic conditions, see text.

between 0.2 to 1.0 μg for glipizide and 0.6 to 1.4 μg for glyburide. The procedure for the extraction of drug from the tablet is very simple and the results of synthetic mixtures indicate quantitative recovery (Tables 1). There was no interference from the excipients present in the tablets including the green and pink colors in glyburide tablets.

The developed methods can be used to determine the content uniformity of the tablets (Table 2). In these studies, the content

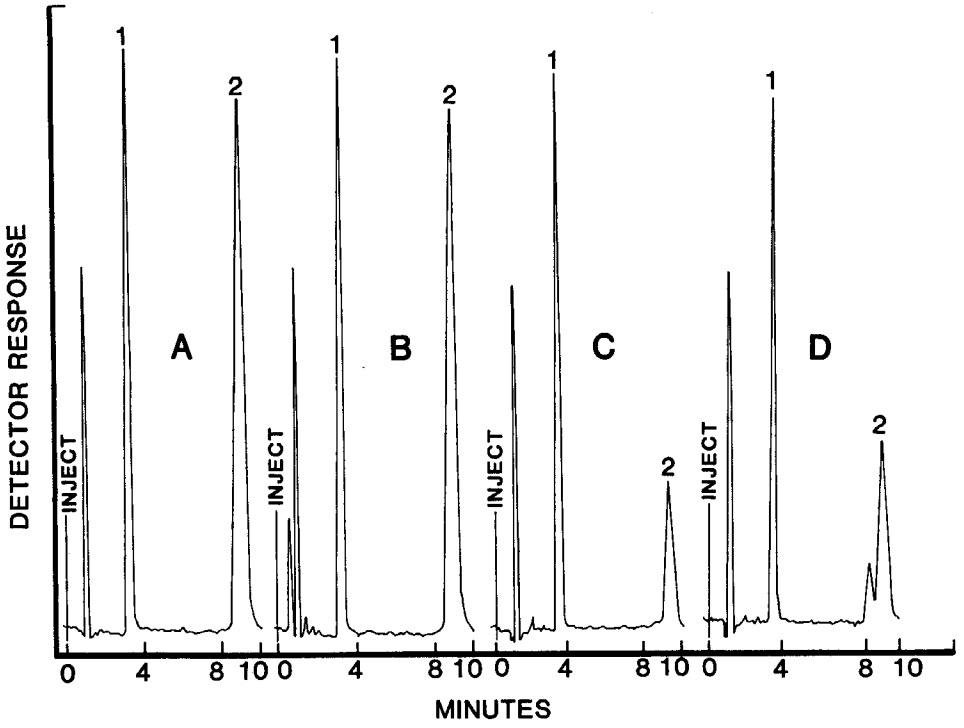

Figure 3 - Sample chromatograms. Peaks 1-2 are from hydrocortisone (the internal standard) and glyburide, respectively. Chromatograms A is from a standard solution; B from 5 mg tablets; C from a solution decomposed with sulfuric acid and D from a solution decomposed with sodium hydroxide. For chromatographic conditions, see text.

uniformity of 5 mg tablets of glipizide and 2.5 mg tablets of glyburide were determined (Table 2). Since, the author did not assay the 1.25 mg tablets of glyburide, the extraction procedure can be modified to test the content uniformity of these tablets by taking one-half of the quantities of methanol and the stock solution of hydrocortisone. The final volume should be made to 25.0 ml instead of 50.0 ml with water.

The separations between the internal standard and the drugs were excellent (Figures 2 and 3). The decomposed solution with sulfuric acid showed one additional peak in the chromatograms (immediately before the intact drug) in both glipizide (Figure 2C) and glyburide (Figure 3C). These additional peaks were very small (Figures 2D and 3D) when the drugs were decomposed with sodium hydroxide solution instead of sulfuric acid. The assay results for glipizide were 46.6% when decomposed with sulfuric acid versus 96.5% when decomposed with sodium hydroxide. The corresponding results for glyburide were 34.5% and 28.7%. Apparently the -NH-CO-NH-group in both drugs (Figure 1) got hydrolyzed.

REFERENCES

(1) Roerig, Inc., New York, NY.

(2) Hoechst-Roussel Pharmaceuticals, Inc., Somerville, NJ.

(3) Microbondapak phenyl, Waters Associates, Milford, MA.

(4) Model ALC 202 equipped with a U6K Universal Injector, Waters Associates, Milford, MA.

(5) Spectroflow monitor SF770, Kratos Inc., Ramsey, NJ.

(6) Omniscribe 5213-12, Houston Instruments, Austin, TX.

(7) Fisher #9-801E, Fisher Scientific Co., Fairlawn, NJ.

(8) Model 4500 Digital pHmeter, Beckman Instruments, Fullerton, CA.