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Direct Spectrophotometric Analysis of Glipizide and Phenformin Hydrochloride in Pharmaceutical Dosage Forms

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Solvent extraction methods followed by spectrophotometric determination of glipizide and phenformin hydrochloride are proposed here. These method are based on the coloured dye-complex formation between acridine yellow and glipizide (AY-G) and brom cresol green and phenformin hydrochloride (BCG-PH) and their extraction by chloroform. The coloured dye complex of AY-G and BCG-PH in chloroform reveal absorption maximum at 426 nm and 415 nm respectively. The system conforms to Beer's law in the range 15 to 100 μg/ml for glipizide and 4 to 24 μg/ml for phenformin hydrochloride. Glipizide and phenformin hydrochloride were determined in pure form first and then in oral hypoglycaemic tablets by proposed methods.

GLIPIZIDE and phenformin hydrochloride are active ingredients of antidiabetic formulations. Therefore rapid, accurate and economic method for their determination is essential. Determination of glipizide in urine of humans by solid-phase extraction followed by its identification with combained TLC and GC/Mass spectrometry is known[1]. Glipizide was also analysed by HPLC in pharmaceuticals[2]. A spectrophotometric method for determination of glipizide in alkaline solution in UV region was reported earlier[3]. Recently, a reversed phase HPLC was employed for determination of phenformin hydrochloride includes colorimetry using brom thymol blue[5] and thymol[6] as chromogenic ligands, Flow injection analysis[7] and HPLC[8]. The extractive spectrophotometric methods employed here are particularly useful because of their simplicity, rapidness, selectivity and yet provides a relatively high degree of accuracy. Glipizide and phenformin hydrochloride were first analysed in pure form by dye complex formation between acridine yellow and brom cresol green respectively. Various optical parameters were ascertained and finally the method was employed for analysis of glipizide and phenformin hydrochloride in pharmaceutical dosage forms.

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Materials and Methods :

About 0.01 g of acridine yellow dye, (GTG England), was dissolved in double distilled water to get 0.02% solution in 50 ml while a 0.5% solution of brom cresol green (Fischer Scientific Co., U.S.A.) was prepared by dissolving 0.25 g in 50 ml of double distilled water. Phosphate buffer of pH 5.8 and potassium hydrogen phthalate-HCl buffer of pH 4.0 were prepared by a method reported earlier[9]. The required quantities of the standard and dosage forms of glipizide (tablets) and phenformin Hydrochloride (tablets and capsules, supplied by U.S.V. Ltd.) were weighed separately and dissolved in A.R. grade methanol (filtered if necessary in the case of tablets and capsules) to get a solution of final concentration of 1 mg/ml. Working standards were prepared by suitable dilution of the stock solutions. All other chemicals used were of A.R. grade. A Systronic MK VI digital pH meter was used for pH measurements

Table 1 : Analysis of glipizide and phenformin hydrochloride working solutions

Weight, (mg)	2	4	6	10
Level of analysis, (μg/ml)	20	20	20	20
Glipizide found, (mg)	1.98	4.03	6.05	9.9
Glipizide Recovery (%)	99.0	100.7	100.8	99.0
Phenformin. HCl found, (mg)	1.99	3.97	5.95	9.98
Phen. HCl Recovery (%)	99.5	99.3	99.2	99.8

and all absorbance measurements were made on GBC 911A UV-VIS Spectrophotometer (Austria).

Method for glipizide determination

Aliquots of the standard solution containing 10-120 μg of glipizide, 1 ml of buffer solution of pH 5.8 and 0.5 ml of acridine yellow were successively added to a series of separating funnel. The contents of each funnel were made upto 5 ml by adding distilled water and then equilibrated for 2 - 3 min with 5 ml of chloroform. After allowing the two phase to settle, the organic phase was separated and its absorbance was measured at 426 nm against reagent blank. A calibration graph was plotted between the concentration of glipizide and absorbance. Aliquots of the sample solution of dosage forms were also treated in a similar manner and the amount of drug present in the sample solution was deduced from the calibration graph prepared earlier.

Method for phenformin hydrochloride determination

Aliquots of standard solution containing 2 - 30 μg of phenformin hydrochloride, 2ml of buffer solution of pH 4.0 and 0.2 ml BCG were added to series of separating funnels. The contents of each funnel were made upto 10 ml and then equilibrated with chloroform for 5 min. The absorbance of the organic phase was measured at 415 nm against reagent blank. Similar procedure was carried out for solution of dosage forms to determine the amount of drug present.

Results and Discussion

It was observed that the AY-G and BCG-PH complexes get extracted in chloroform in the pH range of 4.8-7.0 and 3.5-5.0 respectively. To maintain the reproducibility of the results a buffer solution of pH 5.8 for glipizide and that of pH 4.0 for phenformin hydrochloride extractions were used throughout the experiment. The yellow coloured complex, extracted in chloroform were monitored for several hours after definite time intervals. The AY-G complex was found to be stable for about 72 h and BCG-PH complex for 48 h, with an average absorbance deviation of ±0.005 for both.

The AY-G complex which has an absorption maxima at 426 nm gives linear response for 15 - 100 μg/ml of glipizide concentration. The Sandell's sensitivity (S) and molar absorptivity (ε) were found to be 0 019 μg/ml/cm^2 and 3.68x10^3 l/mol/cm. respectively. Similarly, BCG-PH complex gives linear response for 4-24 μg/ml of phenformin hydrochloride concentration at 415 nm. Sandell's sensitivity (S) and molar absorptivity (ε) for BCG-PH complex were 0.06 μg/ml/cm^2 and 0.67 x 10^3 l/mol/cm respectively.

Effect of various solvents on the extraction of AY-G and BCG-PH complexes were studied and it was observed that apart from chloroform, dichloromethane can also be used as it favours com-

Table 2 : Recovery analysis of glipizide in pharmaceutical dosage form

Sample	Label claim	glipizide content, (mg) Found[a]	Added	Recovered Proposed method	Recovered Official method[10]
Tablet I	5	4.98	3	7.98	7.98
		(99.8)		(99.8)	(99.8)
Tablet II	5	5.0	5	9.95	9.99
		(100)		(99.5)	(99.9)
Tablet III	5	5.06	1	6.02	5.96
		(101.2)		(100.3)	(99.3)

[a]- average of 3 determinations, tablet I and II manufactured by U.S.V. Ltd., tablet III manufactured by Franco-Indian Remedies Pvt. Ltd.
values in parentheses indicate % recovery.

Table 3 : Recovery analysis of phenformin hydrochloride in pharmaceutical dosage form

Sample	Label claim	Phenformin Hydrochloride content (mg) Found[a]	Added	Recovered Proposed method	Recovered Official method[11]
Capsule I	50	49.90	15	64.85	64.95
		(99.8)		(99.8)	(99.9)
Capsule II	50	50.00	40	89.80	89.80
		(100)		(99.7)	(99.7)
Tablet I	25	24.97	25	49.97	49.95
		(99.9)		(99.94)	(99.9)

[a]-average of 3 determinations, all the three samples manufactured by U.S.V. Ltd.
Values in parenthesis indicate % recovery.

plete extraction of both the complexes whereas other solvents such as benzene, toluene, xylene, carbon tetrachloride, hexane and cyclohexane fail to extract these complexes under optimised conditions.

The reproducibility of the method was checked by analysing pure samples of glipizide and phenformin hydrochloride taken from different batches (Table 1). The results were reproducible with average standard deviation of 0.5 % for glipizide and 0.6% for phenformin hydrochloride, (n=5).

In order to validate the proposed methods, recovery studies were conducted by analysing the

pharmaceutical dosage forms in the first instance for the active ingredients by the proposed methods. Then varying amounts of the bulk samples of both the drugs were added to each one of the pharmaceutical dosage form and the total amount of the drug was once again determined by the proposed method after bringing the concentration within Beer's law limits. The results are summarised in table 2 and 3.

The proposed methods are simple, rapid and found to give good recovery results for glipizide (99.6%) and phenformin hydrochloride (99.8%) with low relative standard deviations. The diluents and excipients usually presenting the dosage from did not interfere in the proposed methods. These methods can be used as an alternative to the existing methods.

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