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Simultaneous Spectrophotometric Estimation Of Metformin Hydrochloride And Glipizide In Tablet Dosage Forms

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Abstract: Two sensitive, precise, accurate and simple UV spectrophotometric methods have been developed for simultaneous estimation of Metformin Hydrochloride (MH) and Glipizide (GD) in pharmaceutical dosage forms. Method A involved simultaneous equation method. The two wavelengths 238 nm (λmax of Metformin Hydrochloride) and 275 nm (λmax of Glipizide) were selected for the formation of Simultaneous equations. Whereas method B involved the formation of Q-absorbance equation at isobestic point (259.5 nm). Linearity was observed in the concentration range of 2-10 µg/ml for Metformin Hydrochloride and 1.2-6.0 µg/ml for Glipizide by these methods. The proposed methods have been applied successfully to the analysis of cited drugs in pharmaceutical formulations. Recovery study was performed to confirm the accuracy of the methods. The methods were validated as per ICH guidelines

Keywords: simultaneous estimation, Metformin, glipizide, UV.

Introduction:

Metformin Hydrochloride (MH) and Glipizide (GD) are used in the treatment of Type-II diabetes[1-2].MH is chemically N, N dimethylimido carbonimidic diamide hydrochloride, which improves hepatic and peripheral tissue sensitivity to insulin without the problem of series lactic acidosis. MH is official in BP, Martindale and Merck Index. Literature survey reveals that MH was estimated by HPLC in plasma and urine[3].GD is 1-cyclohexyl-3-[[p-2(-(5 methyl pyrazine carboxamido) ethyl phenyl] sulfonyl urea[4], increases the secretion of insulin by stimulating islet beta cells Several analytical methods were reported for GD using HPLC, UV and LCMS[5-7].GD is official in BP, Merck index, Martindale. More over the literature survey revealed that so far, no method has been reported for estimating MH and GD in combined oral dosage forms using UV Spectrophotometry. It has been used together in combination to achieve better glycolic control and patient compliance. In the present investigation an attempt has been made to develop a simple accurate, reproducible and economical spectrophotometric method for the simultaneous estimation of MH and GD in tablet dosage forms. The pharmaceutical formulations with combinations of drugs have shown an increasing trend to counteract the symptoms specific to one drug and formulation, and hence analytical chemist will have to accept the challenge of developing reliable and easy simultaneous

estimation methods because it does not require manual individual calculations and gives marginally better results.

Experimental:

Materials and Methods

JASCO V-530 UV/VIS double beam spectrophotometer with a pair of 1 cm matched quartz cells was used. Shimadzu BL- 220H analytical balance, MH (Torrent Pharmaceuticals Ltd), GD (Torrent Pharmaceuticals Ltd) and methanol of AR grade (Merck, Mumbai) was used for the study.

Preparation of standard Stock Solution

Standard MH stock solution (100µg/ml): Accurately weighed MH (10mg) was transferred to a 100ml volumetric flask dissolved in methanol to the mark with methanol. Standard stock solutions were further diluted with distilled water to obtain concentration ranges of 2-10 µg/ml

Standard MH stock solution (100µg/ml): Accurately weighed GD (10mg) was transferred to a 100ml volumetric flask and dissolved in methanol to the mark with methanol. Standard stock solutions were further diluted with distilled water to obtain concentration ranges of 1.2-6.0 µg/ml

Analysis of tablet dosage forms Analysis of tablet formulations

For the estimation of drugs from the commercial formulation, twenty tablets of MH and GD in combination was weighed accurately and the average weight per tablet was calculated. Tablets were ground to a fine powder a quantity equivalent to 250mg of MH and 25mg of GD was transferred to a volumetric flask and was extracted with 100ml of methanol. The extract was filtered using whatmann filter paper, and the filtrate was approximately diluted to get a final concentration for both MH and GD The solution was further diluted to get a final concentration of 10µg/ml of the formulation. The absorbance of the solution was measured at 238nm and 275nm.

Method A: Simultaneous Determination

The standard solutions of MH and GD were scanned separately in the range of 200 to 400 nm against methanol as blank and wavelengths of maximum absorbance were determined. The concentrations of drugs were determined using following equations.

$Cx = (A2\times ay1 - A1\times ay2) / (ax2\times ay1 - ax1\times ay2)$

$Cy = (A1\times ax2 - A2\times ax1) / (ax2\times ay1 - ax1\times ay2)$

Where ,Cx = Concentration of Paracetamol in gms/lit
Cy = Concentration of caffeine in gms/lit
A2 =Absorbance at 270nm
A1 =Absorbance at 238nm
ax1= absorptivity of MH at 238 nm
ay1= absorptivity of GD at 238 nm
ax2= absorptivity of MH at 275 nm
ay2= absorptivity of GD at 275 nm

The absorbance of the solution was measured at 238nm and 275nm and concentration of the two drugs was calculated using $C_x = 179.76\ A_2 - 514.12\ A_1/445902.57$—eqn 1 and $C_y = 165\ A_1 - 925.14A_2/445902.57$—eqn 2, where A_1 and A_2 are absorbance of sample solution at 238nm and 275.6nm respectively. C_x and C_y are concentration (in g/100 ml) of MH and GD, respectively in sample solution and calibration curves were plotted. The overlay spectrum of these drugs is shown in Fig. 1. Absorptivity coefficients of two drugs were determined at both wavelengths and two simultaneous equations were formed.238nm (λmax for MH), 275 nm (λmax of GD) and 259.5 nm (isobestic point)

Method B

Absorption Ratio Method (Q Method)

The solutions of MH and GD (10 µg/ml) were scanned in the range of 200 to 400 nm against methanol as blank. For Q method, 259.5 nm (isobestic point) and 275 nm (λmax of GD) were selected as wavelengths of measurements. Concentrations of MH and GD were determined using following equations.

$Cx = (Qm-Qy).\ A1 / (Qx-Qy).\ ax1$

$Cy = (Qm-Qx).\ A1 / (Qy-Qx).\ ay1$

Where $Qm = A2/ A1$
$Qx = ax2/ ax1$
$Qy = ay2/ ay1$

A2= Absorbance of Mixture at 270nm
A1= Absorbance of Mixture at 259.5 nm
ax1= absorptivity of MH at 259.5 nm
ay1= absorptivity of GDat 259.5 nm
ax2= absorptivity of MH at 275 nm
ay2= absorptivity of GD at 275 nm.

Fig :1 Overlay spectra of MH and GD.

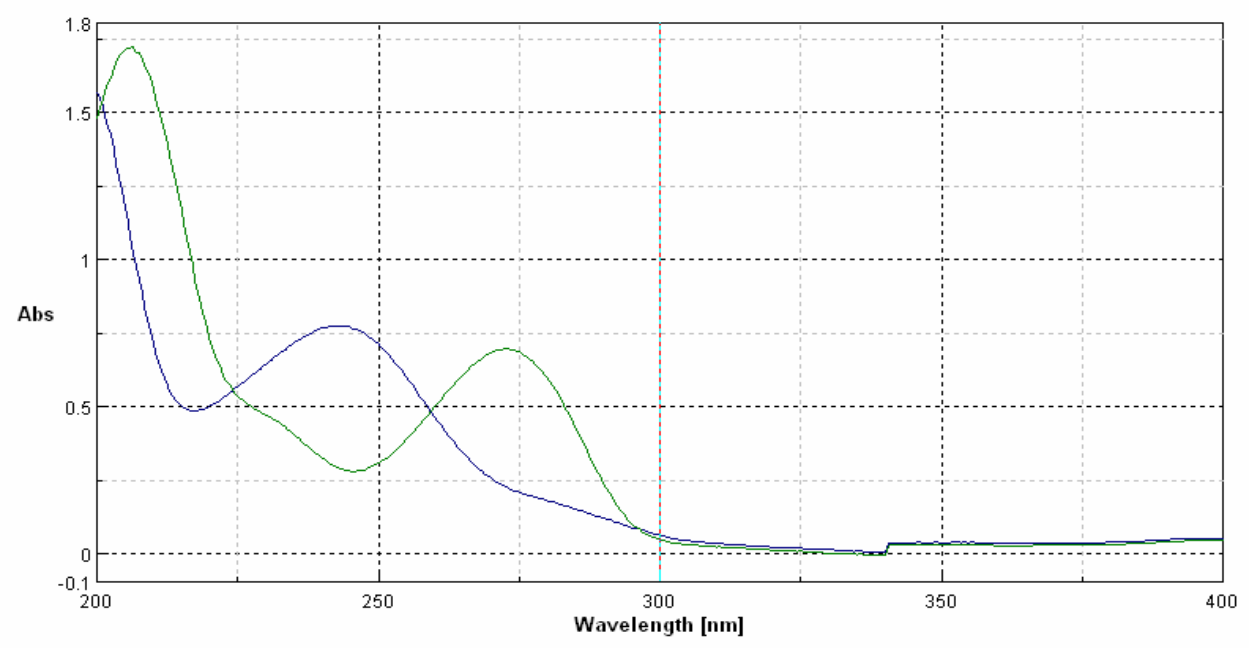

Table: 1 Calibration data for MH and GD for Method A and Method B

Sl. No	Parameters	MH			GD		
		At 238nm	At 275nm	At 259.5nm	At 238nm	At 275nm	At 259.5nm
1	Linearity range µg/ml	2-10	2-10	2-10	1.2-6.0	1.2-6.0	1.2-6.0
2	Slope	0.066	0.015	0.037	0.015	0.050	0.039
3	Correlation Coefficient (R2)	0.999	0.997	0.996	0.998	0.990	0.999

Table 2: Assay results for the determination of MH and GD in tablets by the proposed methods

Sl. No	Drug	Label Claim (µg/ml)	Amount Found (µg/ml)	% label Claim	S. D.	Amount Found (µg/ml)	% label Claim	S. D
1	MH	500	488.64	97.46	± 0.44	470.3	95.46	± 0.33
2	GD	2.5	2.46	99.02	± 0.38	2.42	98.66	± 0.78

Results and Discussion

The proposed methods for simultaneous estimation of MH and GD in combined dosage form were found to be accurate, simple and rapid. The calibration and assay results were depicted in Table 1&2. The % R.S.D. was found to be less than 2, which indicates the validity of method. Linearity was observed by linear regression equation method for MH and GD in different concentration range. The assay results obtained by proposed methods were precise; hence it can be used for routine analysis of two drugs in combined dosage forms. There was no interference from tablet excipients in these methods. Both methods are accurate, simple, rapid, precise, reliable, sensitive, reproducible and economic and are validated as per ICH guidelines.

Conclusion

A simple UV spectrophotometric method was developed for the simultaneous determination of MH and GD in bulk and tablet formulation without any

interference from the excipients. The results of our study indicate that the proposed UV Spectroscopic methods are simple, rapid, precise and accurate. Statistical analysis proves that, these methods are repeatable and selective for the analysis of MH and GD. It can therefore be concluded that use of these methods can save much time and money and itcan be used in small laboratories with accuracy.

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