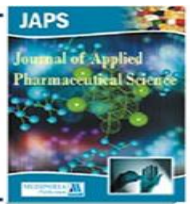
Journal of Applied Pharmaceutical Science
Available online at www.japsonline.com



ISSN: 2231-3354
Received on: 11-05-2012
Revised on: 17-05-2012
Accepted on: 23-05-2012
DOI: 10.7324/JAPS.2012.2738

Development and Validation of Analytical Method for Quantitative Estimation of Miglitol and Metformin in Combined Dosage Form

Sejal R Patel, Prachi V Kabra, Ritu V Kimbahune, Ravikiran Markad and LVG Nargund

Sejal R Patel, Prachi V Kabra, Ravikiran Markad, LVG Nargund
Department of Quality Assurance, Nargund college of pharmacy, Dattatreyanagar, II-main, 100ft ring road, BSK III-stage, Bangalore-85, Karnataka.

Ritu V Kimbahune
Department of Quality Assurance, Al-ameen College of Pharmacy, Hosur Road, Near Lalbagh Main Gate Sudhama Nagar, Bangalore, Karnataka 560 027

For Correspondence
Prachi V Kabra
Department of Quality Assurance, Nargund college of pharmacy, Dattatreyanagar, II-main, 100ft ring road, BSK III-stage, Bangalore-85, Karnataka.

ABSTRACT

A simple, accurate, economical and reproducible UV spectrophotometric method for simultaneous estimation of Miglitol and Metformin in combined tablet dosage form has been developed. The developed method employs multi component spectroscopy using 300nm, 270nm, 240nm and 210nm as wavelengths for estimation. Miglitol and Metformin were found to be linear in the concentration range of 0.2-1.2 µg/ml and 2-12 µg/ml respectively. %Assay was found to be in the range of 99.27 – 99.92% and 99.29 – 99.97% for Miglitol and Metformin respectively. Results of analysis were validated statistically in accordance with ICH guidelines.

Keywords: Miglitol, Metformin, Multi Component Spectroscopy.

INTRODUCTION

Miglitol (MIG) is chemically (2R, 3R, 4R, 5S)-1-(2-hydroxyethyl)-2-(hydroxy methyl) piperidine-3, 4, 5-triol an oral anti-diabetic drug. It reversibly inhibits membrane-bound intestinal alpha-glucosidehydrolyze enzyme which hydrolyzes oligosaccharides and disaccharides to glucose and other monosaccharides in the brush border of the small intestine. In diabetic patients, this enzyme inhibition results in delayed glucose absorption and lowering of postprandial hyperglycemia. Metformin (MET) is chemically N, N-dimethylimidodicarbonimidicdiamide. Itis a biguanide class of oral anti-diabetic drugs. It improves hyperglycemia primarily through its suppression of hepatic glucose production and activates AMP-activated protein kinase. It also increases insulin sensitivity, fatty acid oxidation, peripheral glucose uptake and decreases absorption of glucose from the gastrointestinal tract. In literature, HPLC-UV-MS (Dia *et al.*, 2010), Force degradation study (Chittora *et al.*, 2009)and LC-MS (Xin *et al.*, 2007) methods for estimation of MIG have been reported. Many analytical methods like Spectrophotometric method (Mubeen *et al.*, 2010) available for estimation of MET individually and HPLC methods in combination with Glicazide (Dhable *et al.*, 2010), Pioglitazone (Lakshmi *et al.*, 2009, Sahoo *et al.*, 2009), Repaglinide (Patel *et al.*, 2007), Potentiometry, Spectrofluorimetry and UV-Visible Spectrophotometry, Stability indicating Capillary Electrophoresis (Hamdan *et al.*, 2010) are available in the literature.

As there is no analytical method reported for quantitative estimation of MIG and MET in combination, the present study was aimed for the simultaneous estimation of Miglitol and Metformin by using multi component mode of analysis without prior separation in pharmaceutical dosage form.

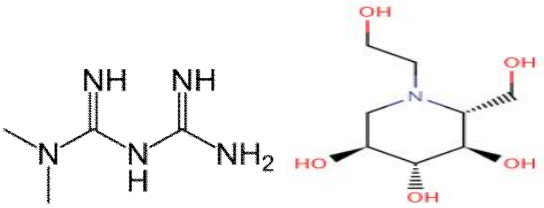


Fig. 1: Structures of Miglitol and Metformin, MiglitolMetformin.

MATERIALS AND METHODS

Reagents and Materials

Miglitol and Metformin in the form of gift samples were kindly supplied by Biocon and Micro Labs Ltd, Bangalore respectively. Double distilled water was used as solvent throughout the study. A combination of Miglitol (50 mg) and Metformin (500 mg) in tablet formulation was procured from local pharmacy (Mignar 50-MF Glenmark Ltd).

Table. 1: Assay of Marketed Formulation (Mignar 50-MF).

Analyte	Lable claim per tablet (mg)	Mean Amount Found in tablet (mg)	Mean Amount found (%)	R.S.D. (%) n=6
MIG	50	49.88	99.76%	0.83
MET	500	498.82	99.77%	0.83

Instrument

A Shimadzu UV/Visible double beam spectrophotometer (Model 1700) with 1cm matched quartz cells was used in present study for multi component analysis.

Method

Five mixed standards of these two drugs were prepared so as to contain 2-10 µg/ml of MET and 0.2-1µg/ml of MIG in double distilled water. All mixed standard solutions were scanned over the range of 300nm to 200nm in multi component mode of spectrophotometer at medium scanning speed with measuring wavelength interval of 30nm. An overlain spectrum of mixed standard solutions is as shown in (Fig 2). The spectral data of these scans were stored in the instrument and used to determine the concentration of two drugs in the sample solution.

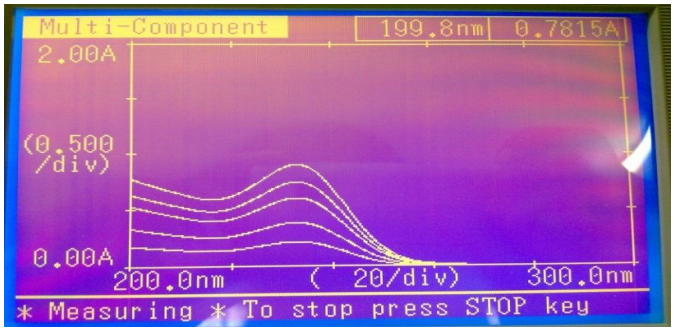


Fig. 2: Overlain spectra of mixed standards of Miglitol and Metformin

Analysis of Commercial Formulation

Twenty tablets were accurately weighed and crushed to fine powder. The tablet powder equivalent to 100mg of MET was accurately weighed, transferred to 100ml volumetric flask, dissolved in small quantity of double distilled water and finally made up to mark withdouble distilled water. This solution was filtered through whattman filter paper No. 41. The filtrate was further diluted with double distilled water to get concentration of 6 µg/ml of MET and 0.6µg/ml of MIG.

The sample solution was scanned over the range of 300nm to 200nm in multi component mode immediately after scanning of mixed standard solutions and concentration of each component was estimated by analysis of spectral data of sample solution with respect to that of mixed standards by the instrument. The spectrum of sample solution is given in (Fig 3).

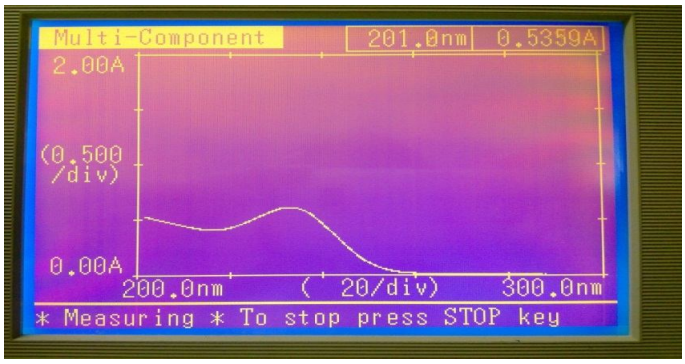


Fig. 3: Spectrum of sample solution.

Validation of Method

Developed analytical method was validated in accordance with ICH guidelines (Q2A).Recovery studies were carried out by addition of pure drug to previously analyzed tablet sample at three different concentration levels (80%, 100% and 120%). The results of recovery studies are reported in Table-2. While precision of the method was determined by repeatability and intermediate precision (inter-day,intra-day) and expressed as %relative standard deviation (RSD). Intra-day precision was evaluated by analyzing concentration of MIG (0.6µg/ml) and MET (6µg/ml) of standard and sample solutions at three different time intervals under the same experimental conditions on the same day. Intermediate precision (inter-day precision) was determined by analyzing above mentioned concentrations of solutions on three consecutive days (Table 3).

Table. 2: Results of Recovery Stydies.

Analyte	LEVEL OF RECOVERY		
	80% (±RSD)	100% (±RSD)	120% (±RSD)
MIG	100.13 ±1.36	99.82 ±1.19	99.523±1.12
MET	100.12 ±0.31	99.81 ±0.54	99.53 ±0.65

Table. 3: Results of Precision Studies (Intra-Day Andinter-Day).

Analyte	Concentrations of sample solution (µg/ml)	Intra-day precision % RSD (n=3)	Inter-day precision % RSD (n=3)
MIG	0.6	1.182066	1.39
MET	6	1.178604	1.38

RESULTS AND DISCUSSION

For selection of solvent, considering the common solubility of drugs, the stock solution was prepared in water while further dilutions were made in different solvents like methanol and glacial acetic acid. Results obtained were found to be satisfactory in water. Hence water was used as solvent throughout the experiment.

As the proposed method is specific to instrument having software for provision of such determination, selection of proper sampling wavelength and concentration of mixed standard are critical. Hence overlay spectra of analytes were studied carefully. Miglitol was found to be absorbing prominently at 200nm in the range of 300nm-200nm while Metformin absorbed at 232nm (λmax)hence, scanning range of 300nm to 200nm was selected for the multicomponent analysis.

The content of analytesin the marketed formulation was found to be99.76% and 99.77% while recovery was found to be 99.5% and 100.1%for Miglitol and Metformin respectively. The values of relative standard deviations of inter-intraday studies were found to be less than 2%. The assay and validation results confirmed that the contents of MIG and MET estimated in the tablet dosage form were free from the interference of excipients.

CONCLUSION

The developed multi component spectroscopy method for simultaneous estimation of Miglitol and Metformin in combined tablet dosage form is simple, economical, accurate and reproducible and can be conveniently adopted for the routine quality control analysis from its pharmaceutical formulations and bulk drug.

REFERENCES

Agarawal YK, Gogoi PJ, Manna K, Bhatt HG, Jain VK. A supercritical fluid chromatography/tandem mass spectrometry method for the simultaneous quantification of metformin and glicaside in human plasma.Indian J pharm sci 2010; 72: 50-7.

Arayne MS, Sultana N, Zuberi MH, Siddique FA.Spectrophotometric quantitation of metformin in bulk drug and pharmaceutical formulations using multivariate technique.Indian J Pharm Sci. 2009; 71: 331-35.

ChittoraNC, Shrivastava A, Jain A. New RP-HPLC method of miglitol in tablet dosage form including forced degradation studies and estimation in spiked rabbit plasma.J Young Pharmacists. 2009; 1(4): 364-70.

Dai XM, Ning AN, WU IM, Li HY, Zhang QM.Development and validation of HPLC-UV-MS method for the control of four anti-diabetic drugs.Acta Pharm Sin. 2010; 45: 347-52.

Dhable PN and Seervi CR. Simultaneous UV spectrophotometric method for estimation of gliclazide and metformin hydrochloride in tablet dosage form. Int J ChemTech Res. 2010 April-June; 2(2): 813-17.

Hamdan II, Bani AKJ and Abushoffa AM. Development and validation of a stability indicating capillary electrophoresis method for the determination of metformin hydrochloride in tablets. J pharm biomed anal 2010; 53(5): 1254-57.

http://www.drugbank.com/Miglitol/ (access date Oct 28, 2010).

http://www.wikipedia.org/defination, Metformin/ (access date Oct 28, 2010).

Jain D, Jain S, Jain D, Maulik A. Estimation of metformin hydrochloride, pioglitazone hydrochloride and glimepiride by RP-HPLC in tablet formulation. J ChromatogrSci 2008 July; 46(6): 501-04(4).

Kar M and Choudhry PK. HPLC method for estimation of metformin hydrochloride in formulated microspheres and tablet dosage form. Indian J Pharm Sci 2009 May-June; 71(3): 318-20.

Lakshmi KS, Rajesh T, Sharma S. Simultaneous determination of metformin and pioglitazone by reversed phase HPLC in pharmaceutical dosage form. Int J Pharm Pharmaceut Sci. 2009 Oct-Dec; 1(2): 162-66.

Mubeen G, Khalikha N and Vimala MN.Spectrophotometric method for estimation of metformin Hydrochloride.Int J ChemTech Res. 2010 April-June; 2(2): 1186-87.

Patel JR, Suhagia BN and Patel BH.Simultaneous spectrophotometric estimation of metformin and repaglinide in a synthetic mixture by two methods. Indian J Pharm Sci. 2007 Nov-Dec; 69(6): 844-46.

Ramolia C, Dedania Z, Dedania R, Sheth NR, Vidyasagar G, Patel B and Bhatt KK. Simultaneous estimation of metformin hydrochloride, rosiglitazone maleate and glimepiride in pharmaceutical dosage forms by RP-HPLC method. Asian J Research Chem. 2010 Jan-Feb; 3(1): 83-86.

RimawiFAl. Development and validation of an analytical method for metformin hydrochloride and its related compound (1-Cyanoguanidine) in tablet formulation by HPLC-UV.Talanta 2009; 79(5): 1368-71.

Sahoo PK, Sharma R and Chaturvedi SC. Simultaneous estimation of metformin hydrochloride and pioglitazone hydrochloride by RP-HPLC method from combined tablet dosage form. Indian J Pharm Sci. 2008 May-June; 70(3): 383-86.

SMH, Mahmoud WH, Elmosallamy MAF and Othman AHM.Determination of metformin in pharmaceutical preparation using potentiometry, spectrofluorimetry and UV-Visible spectrophotometry. Anal chimActa 1999 Jan; 378(1-3): 299-311.

Wanjari MM, There AW, Tajne MR, Chopde CT and Umathe SN.Rapid and simple RPHPLC method for the estimation of metformin in rat plasma. Indian J Pharm Sci 2008 Mar-Apr; 70(2): 198-2023.

Xin L, Wang Y, Wang J, Fawcett JP, Zhao L, Jingkai G. Determination of miglitol in human plasma by liquid chromatography/tandem mass spectrometry. Rapid communication in Mass spectrometry. 2007 Jan; 21(2): 247-51.

Yardimci C and Ozaltin N. Method development and validation of the simultaneous determination of rosiglitazone and metformin in pharmaceutical by capillaryzone electrophoresis. Anal chimActa 2005 Sep; 549(1-2): 88-95.

\