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Research Article

SPECTROPHOTOMETRIC METHODS FOR SIMULTANEOUS ESTIMATION OF METFORMIN HCL AND FENOFIBRATE IN THEIR SYNTHETIC MIXTURE

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ABSTRACT

Two simple spectrophotometric methods have been developed for simultaneous estimation of Metformin HCl and Fenofibrate from their synthetic mixture. Method-I involved simultaneous equation method and Method-II is the Q-absorbance method. For simultaneous equation method, the absorbances of the standard solutions were taken at two wavelengths 237 nm (λ-max of Metformin HCl) and 288 nm (λ-max of Fenofibrate). For Q-absorbance method, the absorbances of the standard solutions were taken at two wavelengths 237 nm (λ-max of Metformin HCl) and 249 nm (Isoabsorptive point), in methanol. Linearity range was found to be 3-20 µg/ml for Metformin HCl and Fenofibrate in both methods based on the ratio of the two drugs in combined dosage form. The accuracy and precision of the methods were determined and validated statistically. Both methods showed good reproducibility and recovery with RSD less than 2. Proposed methods were found to be rapid, specific, precise and accurate and can be successfully applied for the routine analysis of Metformin HCl and Fenofibrate in pharmaceutical dosage form.

Keywords: Metformin HCl, Fenofibrate, Simultaneous equation method, Q-absorbance method

INTRODUCTION

Metformin HCl (MET) chemically, Hydrochloride salt of N,N-dimethylimidodicarbonimidic diamide[1]. It is anti-diabetic drug, primarily acts by decreasing intestinal absorption of glucose reducing hepatic glucose production and increasing sensitivity thus enhancing peripheral uptake utilization of glucose[2]. Fenofibrate (FENO) chemically, 2-[4-(4-chlorobenzoyl)phenoxy]-2-methyl-propanoic acid, 1-methylethyl ester[3]. It is lipid lowering agent which lowers plasma triglyceride be enhancing lipoprotein lipase synthesis thus increasing very low density lipoprotein (VLDL) catabolish with consequent increase in high density lipoprotein[4]. The fixed dose combination increased patient convenience and improved compliance for patients already stabilized on two medications, FENO and MET which can control both the blood lipids and blood glucose of patients.

MET is official in IP[5], BP[6], and USP[7] while FENO is official in BP[5]. A deep Literature survey shows that combination of these two drugs is not official in any pharmacopoeia and no official or reported method is available for simultaneous estimation of MET and FENO in synthetic mixture. Various reported methods are available for estimation of MET alone such as UV[8], HPLC[9-13], LC/MS[14-16], HPTLC[17], Capillary Electrophoresis[18], Voltametry[19] and in combination with other drugs like UV[20-24], HPLC[24-35], HPTLC[36], LC/MS[37-39], Capillary Zone Electrophoresis[40] while for estimation of FENO alone such as UV[41], HPLC[42-46], UPLC[47], LC-MS/MS[48,49] and in combination with other drugs like HPTLC[50]. In the present investigation an attempt has been made to develop simple, rapid, economic and accurate spectrophotometric method for simultaneous estimation of MET and FENO from their synthetic mixture.

MATERIALS AND METHODS

Instrumentation and Apparatus

A shimadzu model 1600 (Japan) double beam UV/Visible spectrophotometer with spectral width of 2 nm, wavelength accuracy of 0.5 nm and a pair of 10 mm matched quartz cell was used to measure absorbance of all the solutions. Spectra were automatically obtained by UV-Probe system software (UV Probe version 2.10). A Sartorius CP224S analytical balance (Gottingen, Germany), an ultrasonic bath (Frontline FS 4, Mumbai, India) was used in the study.

Reagents and Chemicals

Kindly gifted reference standards of MET (Torrent Pharmaceutical Ltd, Gujarat, India) and FENO (INTAS Pharmaceutical Ltd, Gujarat, India), Laboratory prepared synthetic mixture of MET and FENO, Methanol (AR Grade, S. D. Fine Chemicals Ltd., Mumbai, India) and Whatman filter paper no. 41 (Millipore, USA) were used in the study.

Preparation of solutions and mixture

Preparation of standard stock solutions:

accurately weighed (10 mg) of a standard drugs were transferred in two different 100 mL volumetric flasks, dissolved and diluted in methanol to get 100 µg/mL standard stock solutions each of MET and FENO.

Preparation of Synthetic mixture of FENO & MET:

Placebo powder mixture was prepared by mixing 2 gm magnesium stearate, 2 gm starch, 10 gm talc and 6 gm lactose. Synthetic mixture was prepared by mixing 1 gm placebo powder mixture with 160 mg FENO and 500 mg MET.

Wavelength selection

The working standard solutions of MET and FENO, each of 10 µg/mL were scanned separately in the UV range of 200-400 nm. Spectrum data were recorded at an interval of 1 nm. From the absorption overlain spectra of the both drugs, different wavelengths i.e. λ_1= 237 nm (λ_{max} of MET) and λ_2 = 288 nm (λ_{max} of FENO) for Method-I and λ_1= 237 nm (λ_{max} of Met) and λ_3=249 nm (Isoabsorptive point) for Method-II were selected.

Preparation of calibration curve

From the standard stock solutions, 0.3, 0.5, 1.0, 1.5 and 2.0 mL aliquots of both drugs were transferred in two different series of 10 mL volumetric flasks and volumes were made up to mark with methanol to get working standards having concentration in the range of 3–20 µg/mL for both drugs.

Absorbances of each working standard solution of both drugs were measured at λ_1, λ_2 and λ_3.

In Method-I, three Calibration curves of absorbance Vs concentration were constructed, of which one for MET at λ_1, while two for FENO at λ_1 and λ_2. At λ_2, MET have zero absorbance for any concentration.

In Method-II, three Calibration curves of absorbance Vs concentration were constructed of which two at λ_1 for MET and FENO, while one at λ_3 (i.e. Isoabsorptive point of both drug). From respective calibration curve of both drugs absorptivity values were calculated and used in further calculation of the concentration of both drugs in the synthetic mixture.

Table 1: Regression Analysis Data and Summary of Validation Parameter for the proposed Method-I & II.

Parameters	Method-I			Method-II		
	MET at 237 nm	FENO at 237 nm	FENO at 288 nm	MET at 237 nm	FENO at 237 nm	MET & FENO at 249 nm
Concentration range (µg/mL)	3 – 20	3 – 20	3 – 20	3 – 20	3 – 20	3 – 20
Molar absorptivity (1 mole^{-1} cm^{-1})	2.984	3.254	3.186	3.129	2.864	2.769
Regression equation (y=mx+c)						
Slope (m)	0.0985	0.0237	0.0508	0.0982	0.0240	0.0322
Intercept (c)	0.0063	0.0239	0.0084	0.0060	0.0269	0.0108
Correlation coefficient (r^2)	0.9973	0.9977	0.9998	0.9978	0.9989	0.9988
Robustness (CV, %)	0.58	0.79	0.34	0.63	0.86	1.08
LOD (µg/mL)	0.5	0.5	0.5	0.5	0.5	0.5
LOQ (µg/mL)	1	1	1	1	1	1
Repeatability (n=5) (CV, %)	0.59	1.43	0.52	0.42	0.98	1.04
Precision (CV, %)						
Interday (n =5) (CV, %)	0.47-1.93	0.38- 2.06	0.58 -1.63	0.52 -1.85	0.35- 1.83	0.58- 1.90
Intraday (n =5) (CV, %)	0.56- 1.75	0.32- 1.48	0.38- 1.58	0.35- 1.78	0.28- 1.45	0.32- 1.65

n = number of determinations

Table 2: Results of recovery study by proposed methods

			Std. recovered (mg)		Mean % Recovery ± S.D (n=3)	
Drug	Level	Standard added Method I & II (mg)	Method I (mg)	Method II (mg)	Method I	Method II
MET	I	500	495	506	99 ± 1.55	101.20±1.25
	II	1000	987	1026	98.7 ± 1.86	102.6±1.38
	III	1500	1492	1487	99.40 ± 1.32	99.13±1.55
FENO	I	80	78	82	97.50 ± 1.45	102.5±1.12
	II	160	156	162	97.30 ± 1.18	101.2±1.24
	III	240	244	236	101.6 ± 0.85	98.3±0.98

n = number of determinations

Table 3: Intra-Day Precision data for analysis of MET and FENO by Proposed method (n=5)

Conc. (µg/mL)	MET at 237 nm		FENO at 237 nm		FENO at 288 nm		MET & FENO at 249 nm	
	Mean ± S.D. (n=5)	% CV	Mean ± S.D. (n=5)	% CV	Mean ± S.D. (n=5)	% CV	Mean ± S.D. (n=5)	% CV
3	0.272 ± 0.005	1.38	0.022 ± 0.003	1.18	0.104 ± 0.002	0.38	0.055 ± 0.004	1.32
5	0.468 ± 0.006	0.56	0.074 ± 0.004	0.88	0.192 ± 0.006	0.68	0.132 ± 0.002	0.95
10	0.915 ± 0.004	1.65	0.148 ± 0.002	1.48	0.386 ± 0.003	1.15	0.239 ± 0.004	0.32
15	1.412 ± 0.004	1.75	0.376 ± 0.005	0.32	0.590 ±0.005	1.49	0.379 ± 0.003	1.28
20	1.752 ± 0.002	0.83	0.512 ± 0.003	0.64	0.808 ±0.004	1.58	0.511 ± 0.004	1.65

n = number of determinations

Table 4: Inter-Day Precision data for analysis of MET and FENO by Proposed method (n=5)

Conc. (µg/mL)	MET at 237 nm		FENO at 237 nm		FENO at 288 nm		MET & FENO at 249 nm	
	Mean ± S.D. (n=5)	% CV	Mean ± S.D. (n=5)	% CV	Mean ± S.D. (n=5)	% CV	Mean ± S.D. (n=5)	% CV
3	0.267 ± 0.003	1.58	0.020 ± 0.004	1.15	0.101 ± 0.005	0.58	0.052 ± 0.006	1.90
5	0.458 ± 0.005	0.47	0.072 ± 0.002	0.38	0.197 ± 0.005	0.77	0.128 ± 0.003	0.85
10	0.911 ± 0.006	1.65	0.146 ± 0.004	1.47	0.381 ± 0.002	1.45	0.237 ± 0.005	0.58
15	1.409 ± 0.005	1.93	0.376 ± 0.005	2.06	0.594 ± 0.006	1.29	0.376 ± 0.004	1.58
20	1.754 ± 0.003	0.94	0.517 ± 0.005	0.74	0.805 ± 0.003	1.63	0.517 ± 0.006	1.38

n = number of determinations

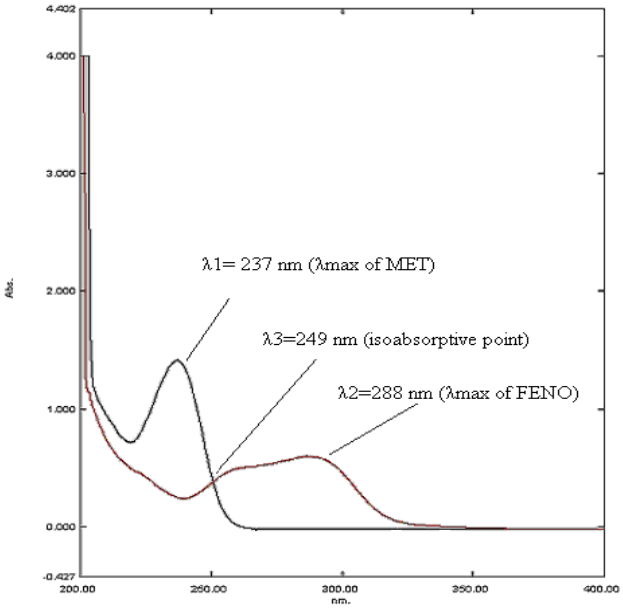

Figure 1: Overlain spectra of MET and FENO

RESULTS AND DISCUSSION

Method Development[51]

From the absorption overlain spectra of standard MET and FENO, the selected wavelengths are shown in Figure1. The overlay spectra pattern of both drug suggests that at $\lambda_{2,MET}$ have zero absorbance for any concentration there is sufficient distance between λ_{max} of both drugs, the criteria run obtaining maximum precision by simultaneous equation method were calculated and found to be outside the range 0.1-2.0. The Isoabsorptive point was found to be 249 nm which was used in Q-Absorbance ratio method.

Calibration curves for MET at λ_1 while for FENO at λ_1 and λ_2 for Method-I, for Method-II at λ_1 and λ_3 for both drugs were constructed and Beer's law range was found to be 3-20 µg/ml at all selected wavelengths for both Methods.

From the respective calibration curves and regression equation, the calculated absorptivity value were found to be ax_1= 950, ax_2=0, ay_1= 240, ay_2=508 for Method-I and a_1x= 890, a_2x=a_2y= 270, a_1y= 185 for Method –II.

The calculated absorptivity values at particular wavelength were substituted in the equations for Method-I and II and concentration of both drugs from synthetic mixture was found out.

For Method-I:

$Cx = (A_1\, ay_2 - A_2\, ay_1) / (ax_1\, ay_2 - ax_2\, ay_1)$ (1)

$Cy = (ax_1\, A_2 - ax_2\, A_1) / (ax_1\, ay_2 - ax_2\, ay_1)$ 2)

Where,

C_X and C_Y = the concentration of MET and FENO, respectively.

A_1 =absorbance of mixture at λ_1

A_2 =absorbance of mixture at λ_2

ax_1 = absorptivity value of the MET at λ_1

ax_2= absorptivity value of the MET at λ_2

ay_1= absorptivity value of the FENO at λ_1

ay_2= absorptivity value of the FENO at λ_2

For Method-II:

$C_X = (Q_m - Q_y) \times A / (Q_X - Q_Y) \times ax_1$ ----- (3)

$C_Y = (A/ax_1) - C_X$ (4)

Where,

C_X and C_Y = the concentration of MET and FENO, respectively.

A = the absorbance of mixture at Isoabsorptive point (λ_3)

ax_1 = absorptivity of MET at Isoabsorptive point (λ_3)

Q_X = (absorptivity at Isoabsorptive point, λ_3)/(absorptivity of MET at λ_1)

Q_Y = (absorptivity at Isoabsorptive point, λ_3)/(absorptivity of FENOe at λ_2)

Q_m = (absorbance of the FENO at λ_2)/(absorbance of the MET at λ_1)

Validation of Method[52]

Linearity:

Both methods were found to be linear over the range of 3-20 µg/mL for the both drugs at all selected wavelengths with the values of correlation coefficient (r^2) > 99. The regression analysis data and optical parameters of both methods were shown in table 1.

Accuracy:

To check the accuracy of proposed methods, multilevel recovery study by standard addition method in placebo powder mixture was carried out. After mixing spiked standard drug at each level were ultrasonicated for 30 min and extracted in methanol. The solutions were filtered through Whatman filter paper No. 41. Suitable aliquots of filter at each level were diluted to get final solutions at each level. Absorbances of final solutions were measured at selected wavelengths for Method I & II and concentrations of both drugs were calculated by using respective regression equations. The results of multilevel recovery study for both methods were shown in Table 2. From the results it can be concluded that both developed methods were accurate.

Method Precision (Repeatability):

Repeatability of measurement of absorbance at selected wavelengths for both drugs using both method were evaluated using 5 replicates of the same concentration (10 µg/mL of MET and FENO). The calculated CV, % value for method precise was found to be within limit as shown in Table 1, suggested that both methods were repeatable.

Intermediate Precision:

The intra-day and inter-day variation of both methods were evaluated at 5 different concentration levels (3, 5, 10, 15 and 20 µg/mL) for both drugs. The percentage Co-efficient of Variance (CV, %) values of within-day and day-to–day were calculated. The results of intra and inter-day variation are depicted in Table 3 and 4, respectively. The CV, % value for day to day and within day was found to be within limit suggested that both methods were sufficiently precise over the calibration range.

Limit of detection (LOD) and Limit of quantitation (LOQ):

LOD was checked by visual method as per ICH guidelines. The values of LOD and LOQ were found to be 0.5 and 1.0 µg/mL (Table 1), for both drugs in both developed methods reveals that purposed method can be applied at low concentration level with sufficient sensitivity.

Robustness:

The study was carried out by change in selected wavelengths for 0 ± 0.1, 0.2, 0.3, 0.4 and 0.5 nm and the CV, % values were calculated, which were found to be less than 2 %. The results suggested that method was robust under experimental conditions.

CONCLUSION

Both developed methods have linear response in the stated range for both drugs and are accurate, precise simple and rapid. The developed methods can be readily carried out at laboratory level and small scale industries using inexpensive instrument i.e. UV/Visible Spectrophotometer. In Future, both methods can be routinely used as quality control of MET and FENO from their combined dosage forms.

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REFERENCES

1. Budavri S. The Merck Index. An Encyclopedia of Chemicals, Drugs, and Biologicals. NJ: Whitehouse Station, Merck & Co., Inc; 2006: 1025.
2. Tierney LM, McPhee SJ, Papadakis MA. Current medical Diagnosis & Treatment. International edition. NY: Lange Medical Books/McGraw-Hill; 2002: 1203-15.
3. Budavri S. The Merck Index. An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station NJ: Merck & Co., Inc; 2006: 679-680.
4. Frederickson DS, Lee RS. A system for phenotyping hyperlipidemia. Circulation 1965; 31: 321-327.
5. Government of India. Ministry of health and family welfare. Indian Pharmacopoeia Vol. I & II. The Controller of Publication, New Delhi; 2007: 1359-1361.
6. British Pharmacopoeial Commission. British Pharmacopoeia Vol-I & II. Controller of Her majesty's stationary office, London; 2005: 811-12, 1292-1293.
7. The USP Convention Inc. United States Pharmacopoeia 28th Ed., 12601 Twinbrook Parkway Rockville, MD; 2005: 1231-1232.
8. Ashour S, Kabbani R. Direct spectrophotometric determination of metformin hydrochloride in pure form and in drug formulations. Taylor & Francis, Philadelphia 2003; 36: 361-370.
9. Chou CH, Cheng CL, Huang CC. A validated HPLC method with ultraviolet detection for the determination of buformin in plasma. Biomed Chromatogram 2004;18: 254-258.
10. Jayasagar G, Krishna Kumar M, Chandrasekhar K, Madhusudan Rao C, Madhusudan Rao Y. Effect of cephalexin on the pharmacokinetics of metformin in healthy human volunteers. Drug Metabol Drug Interact 2002; 19: 41-48.
11. Mooreb GA, Leverc M, Gardinera SJ, Carl M, Kirkpatricka J, Begga EJ. Rapid and simple high-performance liquid chromatographic assay for the determination of Metformine in human plasma and breast milk. Biomed & Pharmacol J 2002; 766:175-179.
12. Charles BG, Jacobsen NW, Ravenscroft PJ. Rapid liquid-chromatographic determination of Metformine in plasma and urine. Clinical Chemistry 1981; 27: 434-436.
13. Wanjari MM, Tajne MR, Chopde CT, Umathe SN. Rapid and simple RPHPLC method for the estimation of Metformine in rat plasma. Indian J Pharm Sci 2008; 70:198-202
14. Wang Y, Tang Y, Gu J, Fawcett JP, Bai X. Rapid and sensitive liquid chromatography-tandem mass spectrometric method for the quantitation of metformin in human plasma. J Chromatogr B Analyst Technol Biomed Life Sci 2004; 808: 215-219.
15. Marques MA, Soares Ade S, Pinto OW, Barroso PT, Pinto DP, Ferreira-Filho M, Werneck-Barroso E. Simple and rapid method determination for metformin in human plasma using high performance liquid chromatography tandem mass spectrometry: application to pharmacokinetic studies. J Chromatogr B Analyt Technol Biomed Life Sci 2007; 852: 308-316.
16. Koseki N, Kawashita H, Niina M, Nagae Y, Masuda N. Development and validation for high selective quantitative determination of metformin in human plasma by cation exchanging with normal-phase LC/MS/MS. J Pharm Biomed Anal 2005; 36:1063-1072.
17. Madhusudan Reddy C, Mubeen G, Pal M. HPTLC method for estimation of metformin hydrochloride. Biomedical & Pharmacology Journal 2008; 15: 228-232.
18. Songa JZ, Chenb HF, Tiana SJ, Suna ZP. Determination of metformin in plasma by capillary electrophoresis using field-amplified sample stacking technique. J Chromatography B: Biomed Sci Appli 1998; 708: 277-283.
19. Skrzypek S, Mirceski V, Ciesielski W, Sokołowski A, Zakrzewski R. Direct determination of metformin in urine by adsorptive catalytic square-wave voltammetry. J Pharm Biomed Anal 2007; 45: 275-281.
20. Jain AK, Agrawal RK. Simultaneous estimation of gliclazide and metformin hydrochloride in combined dosage forms. Indian J Pharm Sci 2002; 64: 88-91.
21. Parikh PP, Mashru RC, Sankalia MG, Sutariya VB. Spectrophotometric determination of olimepimpe and metformin in their combinations. The Indian Pharmacist 2005; 4: 75-78.
22. Patel JR, Suhagia BN, Patel BH. Simultaneous spectrophotometric estimation of metformin and repaglinide in a synthetic mixture. Indian J Pharm Sci 2007; 69: 844-846.
23. Chaturvedi PK, Sharma R. Simultaneous spectrophotometric estimation and validation of three component tablet formulation containing pioglitazone hydrochloride, metformin hydrochloride and glibenclamide. Chromatographia 2008; 41: 2133-2142.
24. Shankar MB, Modi VD, Shah DA, Bhatt KK, Mehta RS, Geetha M, Patel BJ. Estimation of pioglitazone hydrochloride and metformin hydrochloride in tablets by derivative spectrophotometry and liquid chromatographic methods. AOAC Int 2005; 88: 1167-1172.
25. Sahoo PK, Sharma R, Chaturvedi SC. Simultaneous estimation of metformin hydrochloride and pioglitazone hydrochloride by RPHPLC method from combined tablet dosage form. Indian J Pharm Sci 2008; 70: 383-386.
26. Chaturvedi PK, Sharma R. Development and validation of an RP-HPLC method for simultaneous analysis of a three-component tablet formulation containing metformin hydrochloride, pioglitazone hydrochloride, and glibenclamide. J Acta Chromatographica 2008; 20: 451-461.
27. Kolte BL, Raut BB, Deo AA, Bagool MA, Shinde DB. Simultaneous high- performance liquid chromatographic determination of pioglitazone and metformin in pharmaceutical-dosage form. J Chromatogr Sci 2004; 42: 27-31.
28. Gandhimathi M, Anandakumar K, Cheriyan A, Ravi TK. Simultaneous estimation of metformin and gliclazide in tablets using reverse phase high performance liquid chromatography. Indian J Pharm Sci 2003; 65: 530-531.
29. Kolte BL, Raut BB, Deo AA, Bagool MA, Shinde DB. Simultaneous determination of metformin in combination with rosiglitazone by reversed-phase liquid chromatography. J Chromatogr Sci 2004; 42: 70-73.
30. Yardımcı C, Ozaltın N, Gürlek A. Simultaneous determination of rosiglitazone and metformin in plasma by gradient liquid chromatography with UV detection. Talanta 2007; 72: 1416-1422.
31. Najib N, Idkaidek N, Beshtawi M, Bader M, Admour I, Alam SM, Zaman Q, Dham R. Bioequivalence evaluation of two brands of metformin 500 mg tablets (Dialon & Glucophage)--in healthy human volunteers. Biopharm Drug Dispos 2002; 23: 301-306.
32. Yardımc C, Ozaltın N. Simultaneous determination of rosiglitazone and metformin in pharmaceutical preparations by LC. Chromatographia 2007; 66: 589-593.

33. Lad NR, Bhoir SI, Bhoir IC, Sundaresan M. Concurrent assay of metformin and glimepiride in tablets using RP-HPLC with wave length programming. Indian J Pharm Sci 2003; 65: 650-653.
34. Pawar SP, Meshram GA, Phadke MU. Simultaneous LC estimation of glimepiride and metformin in glimepiride immediate release and metformin sustained release tablets. Chromatographia 2008; 68: 1063-1066.
35. Aburuza S, Millership J, McElnay J. The development and validation of liquid chromatography method for the simultaneous determination of metformin and glipizide, gliclazide, glibenclamide or glimperide in plasma. Depart Clinical Pharmacy 2005; 817: 277-286.
36. Ghassempour A, Ahmadi M, Ebrahimi SN, Aboul-Enein HY. Simultaneous determination of metformin and glyburide in tablets by HPTLC. Journal of Chromatographia 2006; 64: 101-104.
37. Zhong GP, Bi HC, Zhou S, Chen X, Huang M. Simultaneous determination of metformin and gliclazide in human plasma by liquid chromatography-tandem mass spectrometry: application to a bioequivalence study of two formulations in healthy volunteers. J Mass Spectrom 2005; 40: 1462-1471.
38. Zhang L, Tian Y, Zhang Z, Chen Y. Simultaneous determination of metformin and rosiglitazone in human plasma by liquid chromatography/tandem mass spectrometry with electrospray ionization: application to a pharmacokinetic study. J Chromatographia B Analyt Technol Biomed Life Sci 2007; 854: 91-98.
39. Mistri HN, Jangid AG, Shrivastav PS. Liquid chromatography tandem mass spectrometry method for simultaneous determination of antidiabetic drugs metformin and glyburide in human plasma. J Pharm Biomed Anal 2007; 45: 97-106.
40. Ceren Y, Ozaltın N. Method development and validation for the simultaneous determination of rosiglitazone and metformin in pharmaceutical preparations by capillary zone electrophoresis. Analytica chimica acta 2005; 549: 88-95.
41. Nakarani NV, Bhatt KK, Patel RD, Bhatt HS. Estimation of atorvastatin calcium and fenofibrate in tablets by derivative spectrophotometry and liquid chromatography. AOAC Int 2007; 90: 700-705.
42. Rani S, Nivsarkar M, Rathod R, Guttikar S, Padh H. Bioequivalence of fenofibrate tablet formulations in health Indian male subjects. Indian J Pharm. Sci 2005; 67: 297-301.
43. Jain N, Raghuwanshi R, Jain Deepti. Development and validation of RP-HPLC method for simultaneous estimation of atorvastatin calcium and fenofibrate in tablet dosage forms. Indian J Pharm Sci 2008; 70: 263-265.
44. Mertens B, Cahay B, Klinkenberg R, Streel B. An automated method for the simultaneous determination of pravastatin, 3-hydroxy isomeric metabolite, pravalactone and fenofibric acid in human plasma by sensitive liquid chromatography combined with diode array and tandem mass spectrometry detection. J Chromatogr A 2008; 1189: 493-502.
45. Straka RJ, Burkhardt RT, Fisher JE. Determination of fenofibric acid concentrations by HPLC after anion exchange solid-phase extraction from human serum. Ther Drug Monit 2007; 29: 197-202.
46. Streel B, Hubert P, Ceccato A. Determination of fenofibric acid in human plasma using automated solid-phase extraction coupled to liquid chromatography. J Chromatogr B Biomed Sci Appl 2000; 742: 391-400.
47. Kadav AA, Vora DN. Stability indicating UPLC method for simultaneous determination of atorvastatin, fenofibrate and their degradation products in tablets. J Pharm Biomed Anal 2008; 48: 120-126.
48. Song M, Hang TJ, Zhang ZX, Du R, Chen J. Determination of cryptotanshinone and its metabolite in rat plasma by liquid chromatography-tandem mass spectrometry. J Chromatogr B Analyt Technol Biomed Life Sci 2005; 827: 205-209.
49. Trivedi RK, Kallem RR, Mullangi R, Srinivas NR. Simultaneous determination of rosuvastatin and fenofibric acid in human plasma by LC-MS/MS with electrospray ionization. J Pharm Biomed Anal 2005; 39: 661-669.
50. Chaudhari BG, Patel NM. Simultaneous estimation of atorvastatin and fenofibrate from formulation by HPTLC. Indian Drugs 2007; 44: 378-383.
51. Davidson AG. Ultraviolet-visible absorption spectrophotometry. In, Beckett AH., Stenlake JB(ed) Practical Pharmaceutical Chemistry. 4th ed., New Delhi: CBS Publishers and distributors, 1997; 286-88.
52. International Conference on Harmonization, Draft Guideline on Validation Procedure, Definitions and Terminology, Federal Register, Fed. 1995; 60: 11260.

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