Review Article

A Review on High Performance Liquid Chromatographic Methods for Oral Hypoglycaemics

S. Nagajyothi*, PV. Suresh, P. Prachat and N. Ramarao

Department of pharmaceutical analysis, Chalapathi institute of pharmaceutical sciences, Chalapathi nagar, Lam, Guntur – 522034, Andhra Pradesh, India.

ABSTRACT

The main goal of this review is to provide overview on the high performance liquid chromatographic methods that are necessary to analyse the oral hypoglycaemic drugs are the **Diabetes mellitus** it is a metabolic dis order characterised by hypoglycaemia, glycosuria, and hyperlipidaemia. **Type 1:-** Insulin dependent diabetes mellitus (IDDM)/juvenile onset diabetes mellitus. There is β cell destruction in pancreatic islets; majority of cases are autoimmune (type 1A) antibodies that destroy βcells are detectable in blood, but some are idiopathic (type1B). **Type 2:-** Non insulin dependent diabetes mellitus (NIDDM/maturity) onset diabetic mellitus. There is a no loss or moderate reduction in βcell mass; insulin in circulation is low, normal or even high ,no antiβcell anti body is demonstrable has a high degree of genetic predisposition generally has a late onset over 90%cases of diabetes are 2DM. These classes of drugs are mainly analysed by using normal phase HPLC in which stationary phase is polar and mobile phase is non-polar. The basic principle of HPLC includes adsorption where the component gets separated based on the relative affinities.

Keywords: HPLC, oral hypoglycimics.

INTRODUCTION

Diabetes mellitus it is a metabolic dis order characterised by hypoglycaemia, glycosuria, hyperlipidaemia. Negative nitrogen balance and sometimes ketonaemia. a wide spread pathological change is thickening of capillary basement membrane increases in vessel wall matrix and cellular proliferation resulting in vascular complications like lumen narrowing, early atherosclerosis ,sclerosis of glomerular capillaries ,retinopathy and peripheral vascular insufficiency.

It having two major types of diabetes mellitus are:

Type 1:-insulin dependent diabetes mellitus (IDDM)/juvenile onset diabetes mellitus.

There is β cell destruction in pancreatic islets; majority of cases are autoimmune (type 1A) antibodies that destroy βcells are detectable in blood, but some are idiopathic (type1B) no βcell antibody is found. In all type 1 cases circulating insulin levels are low or very low and patients are more prone to ketosis. This type is less common and has a low degree of genetic predisposition.

Type 2:-non insulin dependent diabetes mellitus (NIDDM/maturity) onset diabetic mellitus.

There is a no loss or moderate reduction in βcell mass; insulin in circulation is low, normal or even high ,no antiβcell anti body is demonstrable has a high degree of genetic predisposition generally has a late onset over 90%cases of diabetes are 2DM .causes may be :

- Abnormally in gluco-receptor of βcell s so that they respond at higher glucose concentration or relative β cell deficiency in either way insulin secretion is impaired may progress to βcell failure.
- Reduced the sensitivity of peripheral tissues to insulin reduction in number of insulin receptor down regulations of insulin receptors. (1).

CLASSIFICATION OF ORAL HYPOGLYCIMIC DRUGS

Enhance insulin secretion	Overcome insulin resistance	Miscellaneous anti diabetic drugs
1.sulfonylureas Glipizide ,gliclazide, glibenclamide, glimepiride **2.meglatinide/phenylalanine** Repaglinine, nateglytine. **3.dipeptidly peptidase-4** Sitagliptin, vildagliptin saxagliptin, alogliptin, linagliptin. **4. glucagon like peptide 1** Exenatide, liraglutide.	**1.biguanide** Metformin **2.thiazolidinediones** Pioglitazone	**1.α-glycosidase inhibiters** Acarbose, miglitol, voglibone. **2.amylin analogue** Pramlintide. **3.dopamine-D2 receptor** Bromocriptine. **4.sodium-glucose co transport -2** Dapagliflozine.

Table 1: HPLC METHODS ON ORAL HYPOGLYSICEMICS

DRUG NAME	METHOD	STATONARY PHASE	MOBILE PHASE(ratio)	WAVE LENGTH (nm)	FLOW RATE(min)	RETENTION TIME(min)	Class /sub class of drug
Glibenclamide (3)	Rp-hplc	C18(250x6mm ,5µm.	Acetonitrile: phosphate buffer(60:40)v/v	253nm	1ml/min	Less than 12 mins.	K-ATP channel blockers (sulphanyle urea's)
Glipizide (4)	Rp –hplc –uv method	C18(zorbax) ODS 4.6x150nm)	0.01m potassium hydrogen phosphate buffer: acetonitrile (65:35)v/v	275nm	1.5ml/min	Less than 12 min	K-ATP channel blockers (sulphanyle urea's)
Gliclazide (5)	Hplc	C18(250mx4.6 mm)	Methanol: potassium dihydrogen phosphate (85:25)v/v	227nm	1.2ml/min	2.45min	K-ATP channel blockers (sulphanyle urea's
Piogliglitazone hydrochloride (5)	hplc	C18(250mx4.6 mm)	Methanol: potassium dihydrogen phosphate (85:25)v/v	227nm	1.2ml/min	2.42min	Thiazolidinedi one(ppar/activ ar)
Metformin (6)(7)	Rp-hplc	C18(250mx6m m)	Acetonitrile:me thanol:phosph ate buffer(30:60:1 0)v/acetonitrile :water (90:10)v/v	221nm	1ml/min	2.45min&2.74 min.	Biguanide (amp k activer)
Nagateglinide(6)	Rp-hplc	C18(250mx6m m	Acetonitrile:me thanol:phosph ate buffer(30:60:1 0)v/v	226nm	1ml/min	4.22min	Meglitinide/ph enylalanine analogues.
Repaglinide (7)	Rp-hplc	C18	Acetonitrile: water(90:10)v/v	223nm	1ml/min	6.13min	Meglitinide/ph enylalanine analogues.
Saxagliptin (8)	Rp-hplc	C18(5ml/25cm x4.6min)	Phosphate buffer:acetonilr ile:methonol(7 5:15:10)v/v	225nm	1.5ml/min	6.20min	Diphenylpeptid ase-4 (dpp-4) inhibitors.
Metformin pioglitazone(9)	Rp-hplc	Bds(hypercil)c 18 column (250x4.6mm,5 µ)	Acetonitrile: potassium dihydrogen phosphate buffer(50:50)v/v	238nm	1ml/min	Met-2.81min Plo-4.57min	To overcome insulin resistance.
Nateglinide(10)	Rp-hplc	Ace-c18 column (150x4.6mm,5 .0µm)	Acetonitrile:trifl ouroacetic acid(25:25)v/v	210nm	1.5ml/min	7.07min	K-atp channel inhibitors
-Pioglitazone (11)	hplc	C18(3.9mmx1 50mm,5µm)	Ammonium formate buffer is adjusted to formic acid to ph. -3(75:25)	225nm	1ml/min	Less than 12.	To overcome insulin resistance

Natiglinide(12)	hplc	C18(250x4.6mm,5µm)	Methanol:acetonilrile0.05.kh2po4(20:55:25)	215nm	1ml/min	6.040min	Katp-channel inhibitors
Pioglitazone hcl(13)	Rp-hplc	C18(250x4.6mm)	Mixture of buffer :acetonitrile(55:45)v/v	254nm	1ml/min	9.73min	To overcome insulin resistance
Metformin pioglitazone(14)	hplc	C18(150x4.6mm,5µ	Acetonitrile:ammoniumbuffer(42:58)v/v	255nm	0.3ml/min	Met-5.17min Pio-8.1min	To overcome insulin resistance
Natiglinide(15)	Rp-hplc	C18(4.6mmx250mm)	Ammonium dihydrogen phosphate buffer :acetonitrile(40:60)v/v	226nm	1ml/min	4.189min	Meglitinide/phenylalanine analogues.
Metformin&saxgliptin(16)	Rp-hplc	C18(250x4.6mm,5µm	0.05kh2po4"acetonitrile:methanol(60:20:20)v/v	220nm	0.6ml/min	Met-4.38,sax-6.92min	Diphenylpeptidase-4 (dpp-4)inhibitors., Biguanide (amp k activer
Metformin hydrochloride(17)	Hplc-uv	Bio basic scx 5µm,250x4.6mm)	1.7%ammonium di hydrogen phosphate ph-3,v/v	218nm	1ml/min	10.08min	Diphenylpeptidase-4 (dpp-4)inhibitors
Metformin hydrochloride(18)	hplc	Kromasil-c18ODS	Water: methanol(50:50)	270nm	1ml/min	2.3min	Diphenylpeptidase-4 (dpp-4)inhibitors
Tolbutamide(19)	hplc	Rp-18,5µm,	Acetonitrile: ammonium acetate v/v	258nm	1ml/min	Less then 12	Sulfonylureas.
Natiglinide (20)	Hplc-hptlc	C18-(250x4.6mm,5 µm)	Methanol: phosphate buffer(75:25)v/v,(30:70)v/v.	210nm	1ml/min	2.2min	Meglitinide/phenylalanine analogues.
Pioglitazone(21)	hplc	Nova-pak,c18(3.9x150mm	Sodiumphosphate:methanol: acetonitrile(55:30:15)v/v/v	228nm	1ml/min	4.6min	To overcome insulin resistance
Metformin,gliclazide,pioglitazone hydrochloride(22)	hplc	C18 column	Methanol: potassium di hydrogen(85:15)	227nm	1ml/min	Met-2.15min. Gl-3.78min. Pg-4,575min.	Biguanide, thiazolidinedione, sulfonylureas.
Repaginate(23)	hplc	C18(100x4.6nmx5µm)kromasi ODS	Methanol: phosphate buffer/v	242nm	1ml/min	Less than 12 min	Meglitinide /phenylalanine analogues.
Nateglinide(24)	hplc	ODS c18 column	Methanol: phosphate buffer (50:50)v/v	225nm	1ml/min	Less than 12 min.	Meglitinide/phenylalanine analogues.
Pioglitazone (25)	Rp-hplc	C18 column	Methanol:ph4.6 buffer	273nm	1ml/min	Less then 12min.	To overcome the insulin resistance.
Tolbutamide(26)	Rp-hplc	C18 column	Methanol:orthophosphate:acetonitrile(10:30:60)	231nm	1ml/min	4.60min.	Sulfonylureas
Metformin,&Sitagliptin(27)	hplc	BDS-c18 (100x4.6mm)Column	Orthophosphate: methanol(50:50)v/v	215nm	1ml/min	Sit-2.3min,met-4.6min	Diphenylpeptidase-4 (dpp-4)inhibitors., Biguanide (amp k activer
Metformin(28)	hplc	Thermosil ,c18column	Warter:acetonilrile(40:60)	232nm	1ml/min	2.064min	Biguanide (amp k activer)
Nateglinide(30)	Rp-hplc	ACE C18 analytical column (150 x	acetonitrile and0.05% trifluoroacetic	UV detection at 210 nm	1.5 mL/min	7.07 min	Meglitinide/phenylalanine analogues.

		4.6 mm.	acid (25:25v/v)				
pioglitazone and glimepiride(31)	hplc	Inertsil ODS (250 +/-4.6 mm,5micro) column	Acetonitrile and ammonium acetate (pH 4.5; 20mM) in proportion of 60:40 (v/v).	230nm.	1ml/min	Pio-gl 7.0+/-0.1 and 10.2+/-0.1 min	To overcome the insulin resistance. K-ATP channel blockers (sulphanyle urea's
UPLC- (29) **This new Ultra Performance Convergence Chromatography™ (UPC^2 ™) method produced data of equal or better quality than the current HPLC method, was 10 times faster, and consumed less solvent. Column**: ACQUITY UPC2 BEH, 3.0 x 100 mm, 1.7 µm. **Temperature**: 50 °C. **Mobile phase**: 95% Carbon dioxide: 5% methanol/IPA (1:1) containing 0.2% TFA. **Flow rate**: 2.5 mL/min. **Back pressure**: 120 Bar/1740 psi. **Detectio**n: UV /PDA at 254 nm.							

In this HPLC methods mostly using detectors are UV detector and PDA detector.

Conclusion: - oral hypoglycaemic drugs are the **Diabetes mellitus** it is a metabolic dis order characterised by hypoglycaemia, glycosuria, and hyperlipidaemia. Negative nitrogen balance and sometimes ketonaemia. Normal phase HPLC has become important in the analysis of hypoglycimics. This method also helps in studying the reaction mechanisms and also reaction pathways which helps in establishing storage conditions of the drugs

REFERENCES

1. Essentials of medical pharmacology seventh edition KD Tripathi. Oral hypoglycaemic drugs pg.258-259.
2. Pharmacological classification of drugs with doses and preparations KD TRIPATI (5th edition) Pg.42.
3. S.D. rajendra et.al, Indian journal of pharmaceutical sciences rp-hplc method for the estimation of glibinclamide in human serum.
4. Elvester, et.al. Development and validation of RP-HPLC–UV methods for determining of glipizide.
5. Web med central .com, development and validation of hplc method on gliclazide and pioglitazone hydrochloride.
6. Prasanthiet et.al. international journal of pharmacy and pharmacosciences. ISSNO-1491.
7. journal of liquid chromatography and related technologies.volume-35, 2012-ISSUE-3. Vol. 5 | No.2 | 137-141 | April-June | 2012ISSN: 0974-1496 | CODEN: RJCABPhttp://www.rasayanjournal.com.
8. R. Pravin Kumar et.al, Validated RP – HPLC Method For Simuataneous Estimation of Metformin and Saxagliptin in Tablets.
9. Jajow Swapna*et.al. Analytical Method Development and Method Validation for the Simultaneous Estimation of Metformin hydrochloride and Pioglitazone hydrochloride in Tablet Dosage Form by RP-HPLC. ISSN-2231–5667 www.asianpharmaonline.org.ISSN-2231–5675.
10. Aylin HACIOĞLUet.al, Development and validation of an HPLC method for determination ofnateglinide in drug substances Marmara Pharmaceutical Journal 19: 103-108, 2015DOI: 10.12991/mpj.2015199640.
11. AMR Lotfy Saberet.al, Determination of Pioglitazone Hydrochloride in Tablets by High-Performance Liquid ChromatographyISSN-1996-918XPak. J. Anal. Environ. Chem. Vol. 9, No. 2 (2008) 118 . 121.
12. N.V. Krishna Reddyet.al, International Journal of Research in Pharmacy and Chemistry. Available online at www.ijrpc.com, IJRPC 2011, 1(1)validated rp-hplc method for the estimation of nateglinide in formulation.
13. D.Srinivasulu et, al, Development and validation of New RP- HPLC method for determination of Pioglitazone HCl in Pharmaceutical Dosage forms. International Journal of Chemistry Research, Vol 1, Issue 1, 2010.
14. K.S. LAKSHMI et.al international journal of pharmacy and pharmaceutical sciences vol-1, issue-2 simultaneous determination of metformin and pioglitazone by

reversed phase hplc in pharmaceutical dosage forms.
15. Challa Sudheer.et, al, European Journal of Pharmaceutical and Medical Research. www.ejpmr.com *ejpmr, 2016,3(3), 265-270* ISSN 3294-3211. A validated stability indicating rp-hplc method for estimation of natiglinide in bulk and pharmaceutical dosage forms.
16. P. B. N. Prasad1*, K. Satyanaryana2, G. Krishnamohan3,et,alAmerican Journal of Analytical Chemistry, 2015, 6, 841-850Published Online October 2015 in Development and Validation of a Method for Simultaneous Determination of Metformin and Saxagliptin in a Formulation by RP-HPLC. *American Journal of Analytical Chemistry*, 6, 841-850. http://dx.doi.org/10.4236/ajac.2015.61 1080 P. B. N. Prasad1*, K. Satyanaryana2, G. Krishnamohan3.
17. Joanne Gartland, *Thermo Fisher Scientific, Runcorn, Cheshire, UK* Analysis of Melamine and Metformin Hydrochloride by HPLC-UV. www.thermoscientific.com/chromatography.
18. Gadipally Saikiran , et ,al world journal of pharmacy and pharmaceutical sciences. Volume 3, Issue 3, 1149-1159 ISSN 2278 – 4357, method development of metformin hydrochloride rp-hplc.
19. Kuldeep Sharma, et.al, world journal of pharmacy and pharmaceutical sciences.SJIF Impact Factor 5.210Volume 4, Issue 06, 772-783. Research Article ISSN 2278 – 4357. Rp-hplc analytical method for the quantitation of tolbutamide in formulation vehicle: application to homo-gene city and stability evaluation in preclinical study formulation Samples.
20. Manisha S. Phoujdar et, al. effect of ph and role of ionization on Chromatographic performance of nateglinide WORLD JOURNAL OF PHARMACY AND PHARMACEUTICAL SCIENCESSJIF Impact Factor 5,210Volume 4, Issue 06, 1353-1365. Research Article ISSN 2278 – 4357.
21. Rajaa Farhan Husseinet.al. Determination of pioglitazone level and its stability in human plasma by validated hplc assay. world journal of pharmacy and pharmaceutical sciences .sjif impact factor 5.210 volume 4, issue 09, 11-22 research article issn 2278 – 4357.
22. Dr.sunil dhaneshwar, et.al. Article id wwc001078 .Development And Validation of a Hplc Method for the Determination of Metformin Hydrochloride, Gliclazide and Piogliglitazone Hydrochloride in Multicomponent Formulation.
23. PingaleP.et.al, Development and Validation of RP-HPLC Method for the Estimation of Repaglinide in Bulk Drug and Pharmaceutical Formulation. International Journal of Drug Development and Research
24. Madhira vns ram Prasad et.al .International Journal of Scientific & Engineering Research, Volume 5, Issue 4, April-2014 268 ISSN 2229-5518 IJSER © 2014 http://www.ijser.org development and validation of high performance liquid chromatographic method for the determination of nateglinide in human plasma by hplc-uv detection.
25. Ramakrishna Kommana et.al. www.scholarsresearchlibrary.com ISSN 0975-5071. USA CODEN: DPLEB4. Development and validation of HPLC and UV spectrophotometric methods for determination of pioglitazone hydrochloride in bulk and its formulations et.. al of pharmacy and pharmaceutical Sciences, Vol. 1, Issue 2, Oct-Dec. 2009.
26. D. madhulatha et.al, Int. J. Chem. Sci.: 11(4), 2013, 1607-1614ISSN 0972-768X Development and validation of rp-hplc method. For quantitative analysis tolbutamide in pure and pharmaceutical formulations. *www.sadgurupublications.com*
27. KarimUlla S K.et.al. Method development and validation of sitagliptin and metformin using reverse phase HPLC method in bulk and tablet dosage form. . *www.sadgurupublications.com* ISSN 0975-5071 USA CODEN: DPLEB4.
28. Sowjanya P*et.al, rp-hplc method development of metformin in pharmaceutical dosage form. JPA | Volume 4 | Issue 4 | December, 2015(1-19)
29. CIJO MADATHIL XAVIER, et.al, rp-uplc method development and validation for the determination of nateglinide in bulk drug and pharmaceutical formulations: a quality

by design approach. Malaysian Journal of Pharmaceutical Sciences Vol. 10, No. 1, 23–44 (2012).
30. Chromatographic Assay of Tolbutamide Using the ACQUITY UPC System, waters the science of what's possible.
31. Aylin HACIOĞLU, et.al Development and validation of an HPLC method for determination of nateglinide in drug substances Marmara Pharmaceutical Journal 19: 103-108, 2015.DOI: 10.12991/mpj.2015199640.
32. AK, GS, C MR, Bhat K, AR, PM, MS, KK, NU. Pak J Pharm Sci. 2008 Oct; 21(4): 4215. Simultaneous determination of pioglitazone and glimepiride in bulk drug and pharmaceutical dosage form by RP-HPLC method.