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Review Article

A review on analytical methods for determination of oral anti-diabetic drugs like biguanides, gliptins and gliflozins in bulk and in pharmaceutical dosage forms

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ABSTRACT

The aim of this review to focus on a comprehensive update of different analytical methods for determination of oral anti-diabetic drugs for the treatment of type 2 diabetes mellitus (T2DM), such as biguanides, dipeptidyl peptidase 4 inhibitors (gliptins), and sodium/glucose co-transporter 2 inhibitors (gliflozins) in their bulk materials and in pharmaceutical dosage forms. The review entails about analytical procedures like RP-HPLC, HPLC-UV, TLC/HPTLC and spectrophotometric (UV/VIS) methods taken from the literature over the past ten years (2007-2017). This review provides detailed information of estimation and separation conditions for biguanides, gliptins and gliflozins in alone or in combination with or without presence of their impurities and their degradation products.

Keywords: Biguanides; Gliptins; Gliflozins; HPLC; TLC/HPTLC and Spectrophotometric (UV/VS) method

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INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a worldwide problem affecting approximately 8% of the adult population, with predictions of more than 400 million cases by 2030 [1]. The prevalence of T2DM implies an urgent need for new treatments and preventative strategies. The disease results from progressive β cell dysfunction in the presence of chronic insulin resistance, leading to a progressive decline in plasma glucose homeostasis, increased glucagon secretion, gluconeogenesis, and renal glucose reabsorption and reduced incretin response. Treatments recommended by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD) include drugs affecting all of the above processes [2]. In most patients, lifestyle changes and metformin (MET) from biguanides are recommended after diagnosis unless contraindications are present. If the therapeutic goal is not achieved after approximately three months, one of four oral treatment options can be considered in combination with MET: sulfonylureas (SUs), peroxisome proliferator-activated receptor gamma (PPARγ) agonists (glitazones), dipeptidyl peptidase 4 (DPP4) inhibitors (gliptins) or sodium/glucose co-transporter 2 (SGLT2) inhibitors (gliflozins). In patients with contraindications for MET, the initial drug one of these four types of drugs will be the initial treatment option. The choice of the treatment is always based on a particular patient and drug properties, with the goal of improving glycemic control and minimizing side effects [2].

The present review examines analytical methods used for the determination of biguanides, gliptins and glifozins, the second choice drug options for oral treatment, excluding Sulfonylurea and glitazones.

Biguanides: Biguanides (mainly Metformin) are widely prescribed antihyperglycemic agents that suppress hepatic glucose production, increase peripheral glucose uptake, and moderately reduce LDL cholesterol and triglyceride levels. Glucose control with the aid of biguanides appears to decrease the risk of diabetes-related complications, and is not associated with weight gain. The most common adverse effect of biguanides is gastrointestinal distress, including diarrhoea, cramps, nausea, vomiting, and increased flatulence. Long-term use of biguanides has been associated with decreased absorption of vitamin B12 [3]. Metformin is usually prescribed as a single treatment (monotherpay), but it can also be combined with other medication in a single tablet - for example, metformin + pioglitazone (Competact), metformin + vildagliptin (Eucreas), metformin + sitagliptin (Janumet), metformin + dapagliflozin (Xigduo XR). It's also sometimes prescribed in combination with insulin for people with type 1 diabetes [4].

Gliptins: Gliptins represent a novel class of agents that improve beta cell health and suppress glucagon, resulting in improved post-prandial and fasting hyperglycemia. They function by augmenting the incretin system (GLP-1 and GIP) preventing their metabolism by dipeptidyl peptidase-4 (DPP-4). Not only are they efficacious but also safe (weight neutral) and do not cause significant hypoglycemia, making it a unique class of drugs. The main drugs from this group are sitagliptin, vildagliptin, saxagliptin, linagliptin, and alogliptin [5, 6]

Gliflozins: Gliflozins are the newest class of approved oral antidiabetic agents that specifically inhibit sodium-glucose co-transporter 2 function in the kidney, thus preventing renal glucose reabsorption and increasing glycosuria in diabetic individuals while reducing hyperglycemia with a minimal risk of hypoglycemia. They reduce glycated hemoglobin and exert favorable effects beyond glucose control with consistent body weight, blood pressure, and serum uric acid reductions. The main drugs from this group are dapagliflozin, canagliflozin, empagliflozin and ipragliflozin [7-10].

Analytical methods for determination of oral antidiabetics: Pharmaceutical analysis has become one of the most important stages in the therapeutic process. Drug analysis includes analytical investigations of bulk drug materials, the intermediate products, drug formulations, impurities and degradation products. Analytical techniques play a significant role in understanding the chemical stability of the drug, in evaluating the toxicity of some impurities and in assessing the content of drug in formulations. Also, they are fundamental tools in pharmacokinetic studies where the analysis of a drug and its metabolites in biological fluids must be performed. Polypharmacy, which has become an integral part of therapy for many diabetic patients, further supports the importance of drug analysis. To support polypharmacy, methods suitable for two or more components are needed for quality control of such combined formulations as well as for assays in biological samples. This review presents analytical procedures such as HPLC, TLC/HPTLC and spectrophotometric (UV/VIS) methods elaborated for the listed drugs. It is based on a review of the literature from the past ten years (2007-2017).

Table 1: HPLC methods for the analysis of biguanides, gliptins and gliflozins in bulk materials and formulations

Sr. No.	Drug	Sample	Description	Detection mode	Ref. No.
1	Metformin	Bulk substance	**Column :** Inertsil-Extend C18 (250 × 4.6mm, packed with 5µm) **Mobile phase :** 1- Octane sulfonic acid : Acetonitrile (80 : 20) **Flow rate:** 1.0 ml/min **Linearity :** 1 – 250 µg/ml with $r^2 = 0.999$	PDA 232 nm	11
2	Metformin	Tablet dosage form	**Column :** Kromasil -ODS C18 **Mobile phase:** Methanol : orthophosphoric acid (50:50) **Flow rate:** 1.0 ml/min	UV 270 nm	12
3	Metformin	Microspheres and Tablet dosage form	**Column :** Phenomenex C_{18} ODS (5 µ) 250 × 4.60 mm **Mobile phase :** Acetonitrile : phosphate buffer (65:35) pH adjusted to 5.75 with o-phosphoric acid **Flow rate:** 1.0 ml/min **Linearity :** 0 – 25 µg/ml with $r^2 = 0.999$	UV 233 nm	13
4	Sitagliptin	Bulk substance and Tablet dosage form	**Column :** Eclipse XDB C18 column (150.00 mm × 4.60 mm, 5µ) **Mobile phase :** 0.01M Phosphate buffer : methanol (50:50) pH adjusted to 2.5 with orthophosphoric acid **Flow rate :** 0.7 ml/min **Linearity :** 5 – 30 µg/ml with $r^2 = 0.999$ **LOD :** 0.60 µg/ml **LOQ :** 1.9 µg/ml	PDA at 267 nm	14
5	Vildagliptin	Bulk substance	**Column :** Shield C18 column (3.5 µm, 4.6×150mm) **Mobile phase :** 50mM ammonium bicarbonate (pH 7.8) : acetonitrile **Flow rate :** 1.0 ml/min **Linearity :** 10 – 120 µg/ml with $r^2 = 0.997$	UV at 210 nm	15
6	Saxagliptin	Tablet dosage form	**Column :** Kromasil C18 column (150 mm × 4.6 mm i.d., 5 µm) **Mobile phase :** phosphate buffer (pH 4.5) : methanol (65:35) **Flow rate :** 1.0 ml/min **Linearity :** 1 – 10 µg/ml with $r^2 = 0.9899$ **LOD :** 0.10 µg/ml **LOQ :** 0.28 µg/ml	UV at 230 nm	16
7	Linagliptin	Tablet dosage	**Column :** Symmetry C18	UV at 241 nm	17

		form	**Mobile phase** Methanol : water (83:17) **Flow rate :** 1.0 ml/min **Linearity :** 5 – 30 µg/ml with r^2 = 0.999 **LOD :** 0.025 µg/ml **LOQ :** 0.08 µg/ml		
8	Alogliptin	Bulk substance and Tablet dosage form	**Column :** Angilent Zobax SB-CN column (250 × 4.6 mm; 5 µm) **Mobile phase:** Water : acetonitrile : trifluoroacetic acid (1900:100:1) **Flow rate :** 1 ml/min **Linearity :** 5 – 1000 ng/ml with r^2 = 0.9991 **LOD :** 8.32 ng/ml **LOQ :** 24.96 ng/ml	UV at 278 nm	18
9	Canagliflozin	Bulk substance and Tablet dosage form	**Column :** Hypersil BDS, C18 (100 x 4.6 mm, 5 µm) column **Mobile phase:** 0.1% ortho phosphoric buffer : acetonitrile (53:47) **Flow rate :** 1.1 ml/min **Linearity :** 75 – 450 µg/ml with r^2 = 0.9999 **LOD :** 0.23 µg/ml **LOQ :** 24.96 µg/ml	UV at 240 nm	19
10	Dapagliflozin	Bulk substance	**Column :** BDS Column (250×4.5mm, 5µ) **Mobile phase:** Acetonitrile : orthophosphoric acid (55:45) **Flow rate :** 1.0 ml/min **Linearity :** 25 – 150 µg/ml with r^2 = 0.999 **LOD :** 0.6 µg/ml **LOQ :** 1.8 µg/ml	PDA at 245 nm	20, 21
11	Empagliflozin	Bulk substance	**Column :** Intersil column (150x40mm, 5 µm) **Mobile phase:** 0.01 M acetate buffer : methanol (30:70) **Flow rate :** 2.0 ml/min **Linearity :** 2 – 150 µg/ml with r^2 = 0.999 **LOD :** 0.7 µg/ml **LOQ :** 1.91 µg/ml	PDA at 260 nm	22

Table 2: HPLC methods for the analysis of biguanides, gliptins and gliflozins in combined formulations and mixtures

Sr. No.	Drug	Sample	Description	Detection mode	Ref. No.
1	Metformin + Pioglitazone	Tablet dosage form	**Column :** Eclipse XDB plus C18 Column (4.6 × 150 mm, 5µm) **Mobile phase :** Methanol : Tetrahydrofuran (70:30) **Flow rate :** 1.0 ml/min **Retention time :** 1.02 and 2.51 **Linearity :** 10 – 50 µg/ml with r^2 = 0.998 and 10 – 50 µg/ml with r^2 = 0.999 **LOD :** 0.019 µg/ml and 0.010 µg/ml **LOQ :** 0.059 µg/ml and 0.030 µg/ml	UV at 230 nm	23
2	Sitagliptin + Metformin	Bulk substance and Tablet dosage form	**Column :** C18 column (Phenomenex, 250 x 4.6 mm, 5 µm) **Mobile phase :** Phosphate buffer : pH : 4.3 acetonitrile (55:45) **Flow rate :** 1.0 ml/min **Retention time :** 2.34 and 3.20 **Linearity :** 4 – 20 µg/ml with r^2 = 0.997 and 10 – 50 µg/ml with r^2 = 0.998 **LOD :** 1.24 µg/ml and 2.64 µg/ml **LOQ :** 3.76 µg/ml and 8.0 µg/ml	UV at 252 nm	24
3	Vildagliptin + Metformin	Bulk substance and Tablet dosage form	**Column :** Zodiac C18 Column (250 mm X 4.6 mm; 5µm) **Mobile phase :** Phosphate buffer : methanol (73.5 :26.5) **Flow rate :** 1.0 ml/min **Retention time :** 4.243 and 2.490 **Linearity :** 7.5 – 17.5 µg/ml with r^2 = 0.998 and 75 – 175 µg/ml with r^2 = 0.9988 **LOD :** 0.38 µg/ml and 0.09 µg/ml **LOQ :** 1.15 µg/ml and 0.28 µg/ml	UV at 200 nm	25
4	Saxagliptin + Metformin	Bulk substance and Tablet dosage form	**Column :** Enable C18 G (250 × 4.6 mm; 5 µm particle size) **Mobile phase :** 0.05 M KH2PO4 buffer (pH 4.5) : Methanol : Acetonitrile (60 : 20 : 20) **Flow rate :** 0.6 ml/min **Retention time :** 6.92 and 4.38 **Linearity :** 7.5 – 17.5 µg/ml with r^2 = 0.998 and 75 – 175 µg/ml with r^2 = 0.9988 **LOD :** 0.029 µg/ml and 0.112 µg/ml **LOQ :** 0.096 µg/ml and 0.373 µg/ml	UV at 220 nm	26
5	Alogliptin + Metformin	Bulk substance and Tablet dosage form	**Column :** X Bridge C18 column (4.6×150mm), 5µ **Mobile phase :** Buffer : Methanol : ACN (20:60:20) **Flow rate :** 1.0 ml/min **Retention time :** 3.907 and 2.365 **Linearity :** 1.5 – 2.5 µg/ml with r^2 = 0.999 and 60 – 100 µg/ml with r^2 = 0.999	UV at 290 nm	27

6	Canagliflozin + Metformin	Bulk substance and Tablet dosage form	**Column :** Kromosil C18 (250 × 4.6 mm, 5 µm) **Mobile phase :** phosphate buffer : Acetonitrile (65 : 35) **Flow rate :** 1.0 ml/min **Retention time :** 3.57 and 2.43 **Linearity :** 5 – 30 µg/ml with r^2 = 0.9999 and 50 – 300 µg/ml with r^2 = 0.999 **LOD :** 0.361 µg/ml and 0.300 µg/ml **LOQ :** 1.094 µg/ml and 0.910 µg/ml	UV at 248 nm	28
7	Dapagliflozin + Metformin	Tablet dosage form	**Column :** BDS column (250× 4.6mm, 5µ) **Mobile phase :** Phosphate buffer : methanol: acetonitrile (50:30:20) **Flow rate :** 1.0 ml/min **Retention time :** 3.647 and 2.475 **Linearity :** 0.5 – 3 µg/ml with r^2 = 0.997 and 85 – 510 µg/ml with r^2 = 0.997 **LOD :** 0.0365 µg/ml and 0.0247 µg/ml **LOQ :** 0.0365 µg/ml and 0.0247 µg/ml	PDA at 240 nm	29
8	Empagliflozin + Metformin	Bulk substance and Tablet dosage form	**Column :** C18 column (150× 4.6mm, 5µ) **Mobile phase :** Phosphate buffer : methanol (60:40) **Flow rate :** 1.0 ml/min **Retention time :** 4.210 and 2.463 **Linearity :** 3 – 7 µg/ml with r^2 = 0.995 and 60 – 140 µg/ml with r^2 = 0.994	UV at 255 nm	30

Table 3: TLC/HPTLC methods for the analysis of biguanides, gliptins and gliflozins in bulk materials and formulations

Sr. No.	Drug	Sample	Description	Detection wave length (nm)	Ref. No.
1	Metformin	Bulk substance and Tablet dosage form	**Stationary phase :** Silica gel 60 F_{254} **Mobile phase :** Ammonium sulphate (0.5%) :2-propanol: methanol (8.0:1.6:1.6) **Linearity :** 200 – 1000 ng/ml with r^2 = 0.9991 **LOD :** 95 ng/ml **LOQ :** 200 ng/ml	238	31
2	Sitagliptin	Bulk substance and Tablet dosage form	**Stationary phase :** Silica gel aluminium plate 60 F_{254} **Mobile phase :** Toluene : methanol (8:2) **Linearity :** 2000 – 12000 ng/band **LOD :** 193.13 ng/band **LOQ :** 579.18 ng/band	265	32
3	Vildagliptin	Bulk substance and Tablet dosage form	**Stationary phase :** Silica gel aluminium plate 60 F_{254} **Mobile phase :** Ethyl acetate : methanol (8.5:1.5) **Linearity :** 200 –1000 ng/band **LOD :** 61 ng/band **LOQ :** 102 ng/band	217	33

4	Saxagliptin	Bulk substance and Tablet dosage form	**Stationary phase :** Silica gel aluminium plate 60 F_{254} **Mobile phase :** Methanol : Chloroform (6:4) **Linearity :** 400 –1200 ng/band **LOD :** 7.96 ng/band **LOQ :** 26.54 ng/band	222	34
5	Linagliptin	Tablet dosage form and in biological sample	**Stationary phase :** Silica gel aluminium plate 60 F_{254} **Mobile phase :** Methanol : toluene (7:3) **Linearity :** 50 –300 ng/band	232	35
6	Alogliptin	Bulk substance and Tablet dosage form	**Stationary phase :** Silica gel aluminium plate 60 F_{254} **Mobile phase :** Acetonitrile : 1% ammonium acetate in methanol (4.5:5.5) **Linearity :** 100 – 5000 ng/band with $r^2 = 0.999$ **LOD :** 2.356 ng/band **LOQ :** 7.14 ng/band	277	36
7	Canagliflozin	Bulk substance and Tablet dosage form	**Stationary phase :** Silica gel aluminium plate 60 F_{254} **Mobile phase :** Toluene : ethyl acetate : methanol (2:2:1) **Linearity :** 10 – 500 ng/spot with $r^2 = 0.9988$ **LOD :** 0.39 ng/spot **LOQ :** 1.19 ng/spot	290	37

Table 4: TLC/HPTLC methods for the analysis of biguanides, gliptins and gliflozins in combined formulations and mixtures

Sr. No.	Drug	Sample	Description	Detection wave length (nm)	Ref. No.
1	Metformin + Repaglinide	Bulk substance and Tablet dosage form	**Stationary phase :** Silica gel 60 F_{254} **Mobile phase :** Methanol : ammonium sulphate (0.25%) (2.5:7.5) **Linearity :** 500 – 2500 ng/band with $r^2 = 0.9999$ and 100 – 500 ng/band with $r^2 = 0.995$ **LOD :** 98 ng/band and 17 ng/band **LOQ :** 296 ng/band and 51 ng/band	236	38
2	Sitagliptin + Simvastatin	Bulk substance and Tablet dosage form	**Stationary phase :** Silica gel 60 F_{254} **Mobile phase :** Chloroform : methanol (8:2) **Linearity :** 2000 – 7000 ng/spot with $r^2 = 0.9983$ and 250 – 750 ng/spot with $r^2 = 0.9974$ **LOD :** 150 ng/spot and 50 ng/spot **LOQ :** 2000 ng/spot and 660 ng/spot	217	39
3	Vildagliptin + Metformin	Bulk substance and Tablet dosage form	**Stationary phase :** Silica gel 60 F_{254} **Mobile phase :** Ammonium acetate in methanol (1%) : toluene (10:0.5) **Linearity :** 500 – 2000 ng/spot with $r^2 = 0.991$ and 1000 – 5000 ng/spot with $r^2 = 0.999$ **LOD :** 34.60 ng/spot and 17.22	214	40

			ng/spot **LOQ :** 104.85 ng/spot and 52.20 ng/spot		
4	Linagliptin + Metformin	Tablet dosage form	**Stationary phase :** Silica gel 60 F_{254} **Mobile phase :** Acetone : methanol : toluene : formic acid (4:3:2:1) **Linearity :** 20 – 100 ng/spot with r^2 = 0.9993 and 400 – 2000 ng/spot with r^2 = 0.9991 **LOD :** 10 ng/spot and 20 ng/spot **LOQ :** 20 ng/spot and 100 ng/spot	259	41
5	Alogliptin + Metformin	Bulk substance and Tablet dosage form	**Stationary phase :** Silica gel 60 F_{254} **Mobile phase :** Acetonitrile : Ammonium acetate in methanol (1%) (4.5:5.5) **Linearity :** 100 – 2500 ng/spot and 100 – 2500 ng/spot	253	42

Table 5: Spectophotometric (UV/VIS) methods for the analysis of biguanides, gliptins and gliflozins in bulk materials and formulations

Sr. No.	Drug	Sample	Description	Detection wave length (nm)	Ref. No.
1	Metformin	Tablet dosage form	**Solvent :** 0.01N sodium hydroxide **Linearity :** 8 – 13 µg/ml with r^2 = 0.9999 **LOD :** 1.0 µg/ml **LOQ :** 3.0 µg/ml	233	43
2	Sitagliptin	Bulk substance and Tablet dosage form	**Solvent :** Methanol **Linearity :** 20 – 60 µg/ml with r^2 = 0.991 **LOD :** 6.03 µg/ml **LOQ :** 18.28 µg/ml	267	44
3	Vildagliptin	Tablet dosage form	**Solvent :** Water **Linearity :** 12 – 200 ppm with r^2 = 0.999	266	45
4	Saxagliptin	Bulk substance and Tablet dosage form	**Solvent :** Methanol **Linearity :** 5 – 40 µg/ml with r^2 = 0.999 **LOD :** 0.0607 µg/ml **LOQ :** 0.1821 µg/ml	208	46
5	Linagliptin	Tablet dosage form	**Solvent :** Methanol **Linearity :** 5 – 40 µg/ml with r^2 = 0.9985 **LOD :** 0.3649 µg/ml **LOQ :** 1.1059 µg/ml	228	47
6	Alogliptin	Bulk substance and Tablet dosage form	**Solvent :** Water + Bromate – bromide solution **Linearity :** 1 – 10 µg/ml with r^2 = 0.9994 **LOD :** 0.115 µg/ml **LOQ :** 0.348 µg/ml	505	48
7	Canagliflozin	Bulk substance and Tablet dosage form	**Solvent :** Methanol **Linearity :** 5 – 10 µg/ml with r^2 = 0.9989 **LOD :** 0.084 µg/ml **LOQ :** 0.255 µg/ml	290	49
8	Dapagliflozin	Bulk substance and	**Solvent :** Phosphate buffer solution (pH 7.2)	233.65	50

		Tablet dosage form	**Linearity :** 10 – 35 µg/ml with r^2 = 0.9998 **LOD :** 1.24 µg/ml **LOQ :** 3.62 µg/ml		
9	Empagliflozin	Bulk substance and Tablet dosage form	**Solvent :** Ethanol **Linearity :** 2 – 12 µg/ml with r^2 = 0.999 **LOD :** 0.02 µg/ml **LOQ :** 0.07 µg/ml	247	51

Table 5: Spectophotometric (UV/VIS) methods for the analysis of biguanides, gliptins and gliflozins in combined formulations and mixtures

Sr. No.	Drug	Sample	Description	Detection wave length (nm)	Ref. No.
1	Metformin + Pioglitazone	Tablet dosage form	**Solvent :** Methanol **Linearity :** 2 – 10 µg/ml with r^2 = 0.9993 and 2 – 20 µg/ml with r^2 = 0.9996 **LOD :** 0.4 µg/ml and 0.9 µg/ml	225 and 237	52
2	Sitagliptin + Gliclazide	Bulk substances and Tablet dosage form	**Solvent :** Methanol + water **Linearity :** 20 – 100 µg/ml with r^2 = 0.998 and 7 – 27 µg/ml with r^2 = 0.996 **LOD :** 0.23 µg/ml and 0.31 µg/ml **LOQ :** 0.69 µg/ml and 0.93 µg/ml	267 and 226	53
3	Vildagliptin + Metformin	Tablet dosage form	**Solvent :** Water **Linearity :** 60 – 100 µg/ml with r^2 = 0.998 and 10 – 50 µg/ml with r^2 = 0.996 **LOD :** 0.23 µg/ml and 0.31 µg/ml **LOQ :** 0.69 µg/ml and 0.93 µg/ml	218.25 and 225.50	54
4	Linagliptin + Metformin	Tablet dosage form	**Solvent :** Distilled water **Linearity :** 10 – 40 µg/ml with r^2 = 0.999 and 2 – 14 µg/ml with r^2 = 0.999 **LOD :** 1.03 µg/ml and 0.34 µg/ml **LOQ :** 5.18 µg/ml and 1.71 µg/ml	294.4and 230.4	55
5	Alogliptin + Metformin	Tablet dosage form	**Solvent :** Methanol **Linearity :** 0.05 – 0.25 µg/ml with r^2 = 0.9996 and 2 – 10 µg/ml with r^2 = 0.9993	225 and 237	56
6	Dapagliflozin + Metformin	Synthetic mixture	**Solvent :** Methanol **Linearity :** 0.5 – 2.5 µg/ml with r^2 = 0.983 and 25 – 125 µg/ml with r^2 = 0.985	225 and 237	57
7	Empagliflozin + Metformin	Bulk substance and Tablet dosage form	**Solvent :** Methanol **Linearity :** 5 – 25 µg/ml with r^2 = 0.999 and 2 – 12 µg/ml with r^2 = 0.999	272 and 234	58

CONCLUSION

In this literature review, a broad range of analytical methods have been presented for the analysis of oral anti-diabetics in bulk materials and pharmaceutical dosage forms. HPLC with UV detection and UV spectrophotometry were mainly used, due to their accuracy, precision, reliability, repeatability, analysis time and sensitivity. These methods are adequate to analyse the drugs in single component formulation as well as combination preparation. Also, TLC/HPTLC with densitometry detection and VIS spectrophotometry were widely used for typical analysis in pharmaceutical formulation. UV/VIS spectrophotometric methods and TLC/HPTLC methods were frequently

proposed as an alternative to HPLC due to its simplicity and cost effectiveness. Groups of oral anti-diabetics are still extensively developed, and almost every year a new drug similar to these described drugs appears on the market. The analytical methods in this article were gathered together and compared to facilitate steps in designing, in examining, in manufacturing already discovered drugs as well as upcoming new substances.

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