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# SYSTEMATICALLY REVIEWING THE HIGH-PERFORMANCE LIQUID CHROMATO-GRAPHY (HPLC) ANALYTICAL METHODS FOR DETERMINING METFORMIN IN DIFFERENT PHARMACEUTICAL FORMULATIONS AND HUMAN SAMPLES

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**ABSTRACT:** Metformin (MET) is a biguanide class of oral hypo-glycaemic agent which is used in the treatment of diabetes mellitus type II. Currently, MET is the first drug of choice and is primarily prescribed by medical practitioners to at least 120 million people worldwide. The quality-oriented routine analysis of various commercially available products of MET is a major challenge. Several methods have been reported in an industrial scale for thorough quantitative analysis. This review article comprehensively examines the published sophisticated instruments-based nearly 50 analytical methods in various pharmaceutical databases like Google Scholar, PubMed, *etc*. of diverse area of High-Performance Liquid Chromatography (HPLC). The determination of MET in plasma, serum, and urine, extensively requires the HPLC method. For the determination of MET in biological samples, we recommend the LC-MS/MS method since this method combines the HPLC separation ability with MS sensitivity and selectivity, allowing the identification of MET and its metabolites. For pharmaceutical analysis, HPLC with UV detection method is applicable because this method provides accurate results and low cost compared to more advanced detection techniques. This fascinating review comprehensively highlighted the overview of sophisticated analytical techniques for the method development and validation for metformin in the most reliable, accurate, precise, economic, reproducible, and robust manner.

**INTRODUCTION:** Diabetes mellitus (DM) seems to have a high global incidence and death rate, significantly influences people's standard of living, and is regarded as a public health concern. Diabetes mellitus type 2 (DM2), commonly termed as non-dependent diabetes, is by far the most common form of diabetes, accounting for 90 percent to 95 percent of cases.

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Insulin is a hormone generated by the β cell of the pancreas' islets of Langerhans. It is secreted when blood sugar levels rise since insulin is important for the transport and metabolism of carbohydrates to create energy. DM2 is a metabolic disease marked by high levels of sugar in the body, which defects can induce in insulin that leads to the destruction of pancreatic β-cells (insulin producers) or impairment of insulin caused by insulin resistance, among many other things [1].

Polyuria, polydipsia, polyphagia, and accidental weight loss are all clinical signs of diabetes. In most instances, hyperglycemia is asymptomatic and goes untreated until signs of complications appear. The most common DM consequences are ulcers,

amputations, retinopathy, renal failure, and heart disease. The first therapy is centered on lifestyle adjustments, such as increased activity and food modifications, to keep glucose levels below normal limits. If these procedures fail to control blood glucose levels for these criteria, medication intervention is indicated [2].

Such oral antidiabetic representatives or secretagogues (sulphonylureas and methyglinides); insulin secretory sensitizers (thiazolidinediones); neoglycogenesis reducers (biguanidines); and suppressants in the absorptivity of glycines (α-glycosidase inhibitors) are the different types of oral therapeutic drugs. New medications, such as incretinomimetics, antagonists of dipeptidyl peptidase 4 (DPP-IV), and amylin derivatives, have now become accessible to boost effectiveness and lower adverse effects [3].

**Metformin:**

**Description:** Metformin **Fig. 1** belongs to the family of drugs known as biguanides, and it works by lowering glucose synthesis in the liver. Sulfonylureas promote insulin synthesis and include glibenclamide, glimepiride, and gliclazide. Thiazolidinediones improve insulin sensitivity in the liver, adipose tissue, and muscle tissue. Arcabose belongs to the alpha-glucosidase inhibitor family, which reduces glucose uptake in the gut [4].

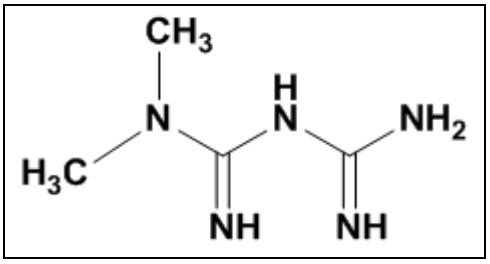


**FIG. 1: STRUCTURE OF METFORMIN**

**Brand Names:** Metformin is available as single-ingredient preparations in Brazil as Dimefor®, Diaformin®, Glicefor®, Formyn®, Gliformil®, Glifage®, Meguanin®, Glucoformin®, Metformed®, Metform®, Metta®, Metformix®, Teutoformin®; in Canada as Glumetza®, Glucophage®, Glycon®; in Germany as Diabesin®, Biocos®, Glucobon®, Diabetase®, Juformin®, Glucophage®, Meglucon®, Mediabet®, Met®, Mescorit®, Metformdoc®, Metfogamma®, Siofor®; in India as Cetapin®, Baymet®, Duomet®, Daomet®, Formin®, Emnorm®, Gluconorm®, Forminal®, Glumet®, Gluformin®, Mefnor®, Glyciphage®, Metafor®, Metaday®, Metatime®, Metanorm®, Metlong®, Metlife®; in Japan as Melbin®, Glycoran®; in the USA as Fortamet®, Glucophage®, Glumetza®, Riomet®; in the United Kingdom as Bolamyn®, Glucophage®, Metabet®, Metsol® [5].

**Applications:** Metformin, a member of the biguanide family, is the preferred therapy for DM2 throughout most individuals since it is more successful. Metformin lowers blood sugar levels while also improving insulin sensitivity. Metformin-assisted therapy lowers microvascular problems by 29% and combined diabetic outcomes by 32%, but insulin and sulphonylureas effectively decrease clinical manifestations by 25% and 12%, respectively. Only extensive metformin medication and intense hypertension management were found to be beneficial in reducing cardiovascular events and death. Metformin, however, does not cause hypoglycemia but does not cause weight gain. Even when administered in clinical circumstances in which it is generally considered inappropriate due to the significant risk of lactic acidosis, it is indeed a lengthy safe medicine [6].

**Action Mechanisms:** Metformin is a drug that is used to manage non-insulin-dependent diabetes that has not responded to diet changes. Metformin is a metabolic inhibitor that affects cellular energy metabolism all over the system. Inhibition of hepatic gluconeogenesis is its principal method of treatment in the condition. Metformin combines with complex I of the mitochondrial electron transport chain, leading cellular ATP levels to drop and AMP to build up. The attachment of AMP to the adenylate cyclase site limits the enzyme's responsiveness to glucagon, causing AMPc-PKA signalling to be disrupted. Consequently, gluconeogenic cascade components are blocked, allowing glycolysis to take over. Metformin lowers hepatic glucose synthesis by this route, which is most likely the principal method of action [7].

**Pharmacokinetics:** Metformin, in the form of hydrochloride salt, is used in medicinal preparations. Metformin has a 40-60% relative oral bioavailability and gastrointestinal absorption is adequate around 6 hours of intake. The negative association between the dosage consumed and the

proportional uptake of recommended levels shows that the saturable absorption mechanism is involved. Metformin is a fast-acting medication that would not attach to plasma proteins. This is not broken down in the liver, and no metabolites or metformin conjugates have been discovered. Metformin is eliminated unaltered in the kidneys and seems to have a plasma elimination half-life of 2 to 6 hours after oral dosing. In individuals experiencing renal dysfunction, its elimination takes longer and is linked to creatinine clearance. Metformin is found in modest levels in human milk [8].

**Physicochemical Properties:** Metformin hydrochloride is a white or almost white crystal, chemically identified as N,N-dimethyl imido dicarbonicar bonide diamide hydrochloride. Its CAS number is 1115-70-4, and its chemical formula is $C_4H_{11}N_5$.HCl. The molecular mass of metformin is 129.16 g/mol, whereas metformin hydrochloride has a molecular mass of 165.6 g/mol. When hydrochloride (1.38 mg/mL), it is readily soluble in water, somewhat soluble in alcohol, and nearly insoluble in acetone and methylene chloride. The melting point is between 223 and 226°C, with a LogP of -0.5 and a pKa of 12.4 (basic). It is administered orally, freely soluble in water, slightly soluble in ethanol and methanol. According to Biopharmaceutics Classification System (BCS), MET is classified under BCS class-III; hence it has high solubility and low permeability. The solubility of the drug was tested in solvents routinely used for analytical methodology. In most cases distilled water and methanol was used as a diluent. The sample preparation techniques for the extraction of MET with acetonitrile, 0.1 N NaOH, 0.1 N HCl, 1% w/v ammonium acetate, benzene, toluene, etc. [9].

**Need for Quality Control:** It is critical to be worried about the need to build successful and trustworthy analytical procedures for quality control since failing to do so might result in catastrophic judgments and irreparable financial difficulties. Metformin is the medicine of choice for DM2, and because of its widespread usage, advanced examination innovations for its assessment and quantification are required. Appropriate analytical techniques will be the first step toward sensible medication usage [10]. Currently, analytical techniques follow the eco-friendly trend, including quick, using no or fewer harmful solvents, miniaturized samples, and decreasing the number of stages and pre-treatments. First suggestions for environmentally benign assessment came in the 1990s due to concerns about the data gained throughout the assessment and even the workers and the ecosystem. Because of worry about the ultimate cost of the goods, environmentally right procedures limit the effects on the environment, the user who communicates closely with the chemicals, and the broader population.

These approaches should have good sensitivity, cheap research costs, low energy usage, clarity, and effectiveness as compared to analysis time. These considerations must be considered throughout the sampling procedure until the ultimate remnant is disposed of. Size reduction of specimens and the replacement of hazardous chemicals are two options for attaining environmentally friendly procedures; nevertheless, this will need adjustments in all analytical processes [11]. The objective of this mini-review is to conduct a discussion on existing analytical methods for the quantification of the MET in a pharmaceutical product.

**Analytical Methods:** Scientific studies and government compendiums were used to explore the analytical procedures for metformin assessment. **Table 1** below illustrates the many analytical techniques for determining metformin reported in the literature. Metformin measurement in tissue specimens is critical for pharmacokinetic research, bioavailability, and bioequivalence, and, consequently, for treatment control of this drug. There is a majority of findings employing HPLC in the studied literature.

It is important to note that there are no analytical techniques or pharmacopeias for tablet form or other pharmaceutical products in the literature; most seem to be exclusively for the raw material. This omission is harmful and may lead to several health care issues. The tablets are the most widely accessible type of metformin.

As a result, the pharmacy sector requires analytical procedures for assessing the finished product's quality prior to its distribution to the mass market.

Items having questionable composition will be discovered on the market if quality control doesn't exist or is inefficient. As a result, patients who do not recover due to their therapy will revert to the healthcare system, which will be overburdened. The kind of analytical procedure is also a concern. The huge pharmaceutical and biotechnology businesses have funds to innovate, while small and medium pharmacy and biochemical enterprises and independent or unaffiliated labs to large corporations do not. As a result, various procedures are required, with the goal of the company or laboratory selecting the best suited approach for their situation. Price is an end item that influences this multidimensional picture. The kind of analysis used has a significant impact on the end product's price. As a result, understanding the consequences of an analysis conclusion is critical.

Most of the procedures investigated do not suit the paradigm of green chemistry since they are hazardous waste sources, such as organic solvents like acetonitrile and methanol. Buffer solutions are not harmful to the environment or the operator. Still, they may shorten the tool's life and accessories like chromatographic columns, which increases the cost of the study. The idea is to attempt to replace the solvent with a less harmful one or to reduce the quantity of solvent used. Analysts and operators, on the other hand, do not strive to modify processes or do not wish to enhance them. Methanol and acetonitrile, for example, are tested immediately and efficiently [12].

Chemicals that are hydrophobic may be first dissolved in ethanol and then diluted in water. This is a regular occurrence in green chemistry labs. The solvent is still utilized, albeit in lesser amounts and with a less harmful solvent. This considers the solvent used for HPLC and the solubility of poorly soluble medicines. During the development of a green approach, attention was paid to using low-toxicity solvents, including the use of low-concentration solvents, as well as the attempt to work with smaller samples via sample downsizing. If that's not practicable, efforts to recover hazardous solvents must be pursued since these substances could be dumped into the environment. Reduced procedures and specimen pre-treatment are indeed form of sustainable chemistry, since these operations have a direct impact on the quantity of chemicals employed, the time it takes to analyse or react, the number of sections needed, and the expense. Absorption spectroscopy in the infrared spectrum is a possibility and a reality for chemical preparations. It may be used to examine raw materials and medications in qualitative and quantitative ways. It is regarded as a superior method of pharmaceutical analysis. By contrasting the spectra of the reference to the spectra of the commodity to be evaluated, spectrophotometry in the infrared region may also suggest the keeping quality be examined, which is regarded as an indicative technique of stability. The selection of devices is also essential; it is suggested to use such that necessitate the lowest quantity of solvent, take less energy for analysis, use less power, lead to losses less money, and produce consistently lower consumer prices, such as high-performance liquid chromatography or capillary electrophoresis. The best technique for any analysis or research should not be the most well-known or widely used approach. It should be the best method for your analysis or study. These approaches' advantages and financial benefits should encourage more people to use them. As a result, universities constitute reference research centers in the field, helping to attain this goal [13].

**TABLE 1: REPORTED HIGH-PERFORMANCE LIQUID CHROMATOGRAPHY (HPLC) METHODS FOR THE QUANTITATIVE ANALYSIS OF METFORMIN IN FORMULATIONS**

| Compound | Sample | Mobile phase | Flow rate (ml/min) | Column | Detector | Wavelength (λmax) | LOD (µg/ml) | LOQ (µg/ml) | Ref. |
|---|---|---|---|---|---|---|---|---|---|
| Glimepiride + metformin | Bulk And Tablet Dosage Form | ACN: Methanol: Potassium Dihydrogen Phosphate (45: 55: 20 v/v/v) | 1 | Hypersil BDS C18 | UV | 238 | - | - | 14. |
| Metformin | Tablet Dosage Form | 10m.mol 1-Octane sulfonic acid: Acetonitrile (80: 20 v/v) | 1.0 | Inertsil-Exd C18 | PDA | 232 | - | - | 15. |
| Metformin | Bulk And Synthetic | Water: CAN (40: 60 v/v) | 1.0 | Thermosil C18 | UV | 232 | - | - | 16. |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | Mixture | | | | | | | | |
| Metformin + Gliclazide | Bulk And Tablet Dosage Form | ACN: PB (85: 15 v/v) | 1.2 | Inertsil-ODS | UV | 227 | 0.1 | - | 17. |
| Metformin + Alogliptin | Bulk And Synthetic Mixture | Methanol | 0.7 | AGLIENT C-18 (250 x 4.6 mm) 5 µm | UV | 242 | - | - | 18. |
| Metformin + Alogliptin | Human Plasma | Sodium dihydrogen ortho phosphate [pH 4.0]: ACN (70: 30 v/v) | 1.0 | X-Terra C18 | UV | 235 | - | 5.936, 1.983 | 19. |
| Metformin + Canagliflozin | Bulk And Synthetic Mixture | Methanol: 0.03 M Phosphate buffer (pH 3.2) | 1.0 | C18 | UV | 240 | - | - | 20. |
| Metformin + Cimetidine + Famotidine + Ranitidine | Human Serum And Dosage Form | Methanol: Water: Triethylamine (20: 80: 0.05 v/v/v), pH 3.0 Phosphoric acid (85%) | 1.0 | Purospher Star RP18 | UV | 229 | 0.071, 0.116, 0.134, 0.110 | 0.217, 0.352, 0.405, 0.368 | 21. |
| Metformin + Empagliflozin | Bulk And Dosage Form | Methanol: PB ($KH_2PO_4$ and $K_2HPO_4$) phosphate (pH 3 adjusted orthophosphoric acid) (70: 30 v/v) | 1.0 | Intersil C18 | PDA | 240 | 2.17, 0.0372 | 6.60, 0.1125 | 22. |
| Metformin + Empagliflozin In | Bulk And Synthetic Mixture | Ortho Phosphoric Acid Buffer: ACN (45: 55 v/v). | 1.0 | Kromosil C-18 | PDA | 233 | 0.48, 0.016 | 1.49, 0.049 | 23. |
| Metformin + Ertugliflozin | Bulk And Dosage Form | Potassium dihydrogen pH 4.0 and methanol (65: 35 v/v) | 1.0 | Inertsil C18 | UV | 220 | 1.04, 9.61 | 0.0007, 0.006 | 24. |
| Metformin + Glibenclamide | | ACN : 0.05 M $KH_2PO_4$ adjust pH 3 phosphoric acid (60: 40 v/v) | 1.0 | C18 | UV | 210, 238 | 0.64 0.02 | 1.95 0.07 | 25. |
| Metformin + Glibenclamide | | Methanol: ACN : Water (60: 20: 20 v/v/v) | 1.0 | Oyster BDS RP- C18 | UV | 228 | - | - | 26. |
| Metformin + Glibenclamide Tablet | Bulk And Tablet Dosage Form | 0.1 M ammonium acetate solution and methanol in a ratio (23: 77 v/v) | 1.2 | Reversed phase C8 | PDA | 230 | - | - | 27. |
| Metformin + Gliclazide | | PB: ACN (55: 45 v/v) | 1.0 | ZODIAC column C18 | UV | 248 | - | - | 28. |
| Metformin + Gliclazide | Bulk And Dosage Form | Methanol, acetonitrile, and Phosphate Buffer pH 5.0 (55: 10: 35 v/v) | 1.5 | Phenomene x C18 | UV | 257 | 1.68, 0.28 | 4.95, 0.79 | 29. |
| Metformin + Glimepiride + Pioglitazone | Tablet Dosage Form | Methanol: phosphate buffer (pH 3.6 adjusted orthophosphoric acid) (75: 25 v/v) | 1.0 | C18 | PDA | 238 | 0.15, 0.02, 0.12 | 0.45, 0.06, 0.36 | 30. |
| Metformin + Glimepiride | | Methanol: phosphate buffer (Ph 4.3) (75: 25 v/v) | 1 | Inertsil-ODS-3 C-18 | UV | 258 | - | - | 31. |
| Metformin + Glimepiride | Tablet Dosage Form | Tween-20: n-butanol: PB (p H 4.2) (50: 25: 25 v/v/v) | 1.5 | Luna C18 | UV | 225 | 0.033 | | 32. |
| Metformin + Linagliptin | | Methanol: 0.05 M potassium dihydrogen orthophosphate (pH 4.6) (70: 30 v/v) | 0.6 | C18 | UV | 267 | 0.0414, 0.07591 | 0.1255, 0.2300 | 33. |
| Metformin + Linagliptin | Human Plasma | ACN: Methanol: 0.01% Formic acid (30: 13.59: 56.41 v/v/v) | 0.892 | Onyx C18 Monolithic | PDA | 220 | 0.0039, 0.0018 | 0.0118, 0.0056 | 34. |
| Metformin + Pioglitazone + Glimepiride | Bulk And Synthetic Mixture | PB: ACN (55: 45 v/v) | 1.0 | ODS, | UV | 230 | - | - | 35. |
| Metformin + Pioglitazone + Glimepiride | Tablet Dosage Form | Potassium dihydrogen phosphate (PB pH 6.8): methanol (40: 60 v/v) | 1.0 | C-18 | UV | 257 | 0.046, 0.005, 0.054 | 0.159, 0.012, 0.172 | 36. |
| Metformin + Pioglitazone + | Tablet Dosage Form | Methanol : phosphate buffer (pH 4.3) (75: 25 | 1.0 | Inertsil-ODS-3 | UV-PDA | 258 | - | - | 37. |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Glimepiride | | v/v) | | (C18) | | | | | |
| Metformin + Pioglitazone + Saxagliptin + Repaglinide + Glimepiride + Gliclazide | Pure Powder | ACN: 0.05 M potassium dihydrogen phosphate and 0.01 M sodium octane sulfonate (pH 3.55) | 0.85 | Kromasil 100-C18 | UV | 220 | 0.001, 0.001, 0.002, 0.003, 0.002, 0.004 | 0.002, 0.003, 0.009, 0.012, 0.007, 0.024 | 38. |
| Metformin + Ramipril + Glim | Bulk And Tablet Dosage Form | Methanol: 0.02 M $KH_2PO_4$ buffer (85: 15 v/v) | 0.8 | Hypersil BDS C18 | UV | 210 | 2.88, 2.88, 2.88 | 8.72, 8.73, 8.72 | 39. |
| Metformin + Repaglinide | | ACN: Methanol (20: 80 v/v) | 1.0 | Devenosil ODS HG-5 RP C18 | UV | 242 | - | - | 40. |
| Metformin + Rosiglitazone | | Sodium dihydrogen PB: ACN (60: 90 v/v) | 0.7 | ODS C18 | UV | _ | | | 41. |
| Metformin + Saxagliptin | | ACN: PB (pH 4.5 ± 0.1 adjusted with orthophosphoric acid) (13: 87 v/v) | 1.5 | Kinetex™ column– C18 | UV | 220 | - | - | 42. |
| Metformin + Saxagliptin | Bulk And Tablet Dosage Form | 0.02 M dipotassium hydrogen orthophosphate (pH 3.3): ACN (40: 60 v/v). | 1.0 | ODS | UV | 260 | - | - | 43. |
| Metformin + Saxagliptin | | PDOP: Methanol (50: 50 v/v) | 1 | Hypersil BDS C18 | PDA | 260 | 1.02 | - | 44. |
| Metformin + Saxagliptin | Tablet Dosage Form | Methanol: ACN: PB(20: 35: 45 v/v/v) | 1.0 | Xterra Symmetry C8 | UV | 254 | 0.24, 0.42 | - | 45. |
| Metformin + Saxagliptin | | PB:ACN (60: 40 v/v) | 1.0 | Hypersil BDS C18 | UV | 260 | - | - | 46. |
| Metformin + Saxagliptin | Bulk And Tablet Dosage Form | Ammonium dihydrogen PB: ACN (74: 26 v/v) | 1 | Inertsil ODS | UV | 246 | 0.06 0.13 | - | 47. |
| Metformin + Saxagliptin | | Water: Methanol (60: | 1.0 | Intertsil-E | UV | 258 | 0.663, 0.405 | 1.92, 1.228 | 48. |
| Metformin + Saxagliptin | Bulk And Synthetic Mixture | 0.05 M $KH_2PO_4$ buffer (pH 4.5): Methanol: Acetonitrile (60: 20: 20 v/v) | 0.6 | Enable C18 G | UV | 220 | - | - | 49. |
| Metformin + Saxagliptin + Atorvastatin | | Buffer: Methanol (30: 70 v/v) | 1 | Hypersil GOLD | UV | 254 | 0.82, 0.4, 0.09 | - | 50. |
| Metformin + Teneligliptin | Tablet Dosage Form | Water (pH 4.0, adjust 1% Orthophosphoric acid): Methanol (60:40 v/v) | 1.0 | C18, Hypersil BDS | UV | 236 | - | - | 51. |
| Metformin + Teneligliptin | Tablet Dosage Form | Methanol: water (OPA 0.05 %) (50:50 v/v) | 1.0 | Agilent C8 | UV | 245 | - | - | 52. |
| Metformin + Teneligliptin | Bulk And Dosage Form | Phosphate buffer (pH 3): Acetonitrile (50: 50) v/v | 1.0 | Inertsil ODS | UV | 240 | 3.00, 3.02 | 9.98, 10.00 | 53. |
| Metformin + Teneligliptin | Bulk And Synthetic Mixture | Orthophosphoric acid buffer (pH 4.0): Acetonitrile : Methanol (30: 30: 40 v/v/v), | 1.4 | Zodiac ODS C18 | UV | 228 | 1.69 0.08 | 5.12 0.24 | 54. |
| Metformin + Teneligliptin | Pure Drug | Methanol: ACN: Potassium dihydrogen orthophosphate (pH 4.6 orthophosphoric acid (40: 20: 40 v/v/v) | 1.0 | C18 Phenomene x Kinetex | PDA UV | 250 | 0.0040, 0.0232 | 0.0122, 0.0703 | 55. |
| Metformin | Human Plasma | 34% ACN: 66% aqueous phase (10 µM $KH_2PO_4$ and 10 µM sodium lauryl sulfate. Aqueous phase pH was adjusted to 5.2) | 1.3 | C-18 | UV | 233 | 0.062 | 0.125 | 56. |
| Metformin + Saxagliptin + | Tablet Dosage Form | ACN and acidic aqueous phase pH 3 (70: 30 v/v) | 1.0 | Agilent C18 | PDA | 230 | - | - | 57. |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Dapagliflozin Metformin + Saxagliptin | Tablet Dosage Form | Methanol: PB (60: 40 v/v) | 1 | Symmetry C18 | UV | 258 | 3.0, 2.9 | - | 58. |
| Metformin + Saxagliptin | Bulk And Synthetic Mixture | 0.02 M $KH_2PO_4$: ACN (55: 45 v/v) | 1 | Phenomenex C18 | UV | 252 | 1.24, 2.64 | - | 59. |
| Saxagliptin + Metformin | Bulk And Tablet Dosage Form | Potassium dihydrogen orthophosphate (pH 8.5): Methanol (50: 50 v/v) | 1.0 | Hypersil BDS C18 | | 215 | - | - | 60. |
| Voglibose + Glimepiride + Metformin | Bulk And Tablet Dosage Form | ACN: PB 85: 15 v/v (pH 4) | 1.0 | ODS C18 | UV | 223 | 0.585<br>0.063<br>0.644 | 0.717<br>0.193<br>0.810 | 61. |

**CONCLUSION:** Metformin is the medicine of preference again for managing diabetes mellitus type 2 (DM2), a condition that has become a global pandemic. The widespread usage of this medicine aids the creation of investigations that require analytical and bioanalytical assessment. Conventional systems for quantifying metformin in raw resources, pharmaceuticals, and biological systems in the research and official compendiums might still consider the idea of green chemistry, whether it's in the selection of solvents, methodology, the quantity of samples, amount of stages, and so on. Analysis techniques must always be constantly improved.

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