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A Simple Review Of Analytical Techniques For Determination Of Metformin And Impurity Profiling Study

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ABSTRACT:

Metformin is an oral anti-diabetic medicine that prevents difficulties of type 2 diabetes. It is an effective first-line therapy for obese individuals with type 2 diabetes and is presently accessible in over 60 countries worldwide.

Oral anti-hyperglycemic medication metformin is frequently used for the treatment of type II diabetes, also known as noninsulin dependent diabetes mellitus (NIDDM). This article highlights a number of analytical techniques, including, analytical method such as Uv Spectroscopy, Hplc, Hptlc, Impurity Study, for the determination of metformin in biological matrices and medicinal formulations . Also including the data regarding impurity study of metformin in corresponding combination

KEYWORDS: METFORMIN HYDROCHLORIDE ,ANALYTICAL METHOD,UV SPECTROSCOPY, HPLC, HPTLC, IMPURITY STUDY

INTRODUCTION:

Worldwide, Type II Diabetes Mellitus is a metabolic disease that poses a serious risk to public health. It is predicted that by 2030, there would be 430 million adults with diabetes worldwide, an increase of 7.7% [1]

Diabetes mellitus (DM) is a form that affects many people's quality of life, is very fatal, and is regarded as a public health issue globally.[2]

Known as non-insulin dependent diabetes, DM type 2 (DM2) is the most collective type of diabetes, accounting for nearly 90–95% of cases [3]

Metformin hydrochloride is a hypoglycemic medication that is a white, crystalline powder that is hygroscopic and freely soluble in water. Its chemical name is 1, 1-dimethyl biguanide hydrochloride. formula for molecules C4H11N5.The metformin drug's structural formula, HCL [4,5], is displayed in Figure 1.

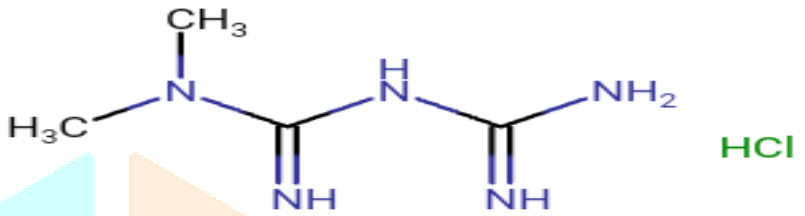

Figure 1. Metformin Hydrochloride

The medication's BAN, USAN, and INN are all referred to as "Metformin". Glucophage XR, Carbophage SR, Riomet, Fortamet, Glumetza, Obimet, Gluformin, Dianben, Diabex, Diaformin, Siofor, Metfogamma, and Glifor are among the brand names under which it is sold. The World Health Organization (WHO) states that it is used as an antihyperglycemic and for the treatment of kind 2 diabetes, which frequently affects people over forty as well as unusual age agencies caused by insulin deficiency due to the presence of Beta cell insufficiency in the pancreas can be caused by the introduction of sites in the body or poor resistance to insulin receptors, particularly in overweight individuals. [6,7]

Metformin hydrochloride is the primary medicine for controlling blood glucose levels in non-insulin-dependent diabetics (type II). Metformin hydrochloride activates AMP-activated protein kinase (AMPK), reducing hepatic glucose synthesis (gluconeogenesis) and so lowering blood glucose levels. It enhanced insulin sensitivity and lowered glucose absorption in the gut, leading to better glucose uptake and utilization at the peripheral level. It affects the mitochondrial respiratory chain, leading to increased anaerobic glycolysis and peripheral glucose use. It promotes weight loss over gain and reduces the incidence of macrovascular and microvascular problems in diabetes patients [8].

PHYSICAL AND CHEMICAL PROPERTIES:

Metformin is a white crystalline powder with the IUPAC name 3-(diamino methylidene)-1,1-dimethylgunidine

The molecular formula C4H11N5 and molecular weight of 129.197g/mol, melting point of 223-226oC.

Metformin has two pKa value:

1] pKa:2.8

2] pKa :11.5 metformin's pKa designates that it will practically totally in ionized form with between in pH value 5-9 and metformin freely soluble in HCl salt, stable under recommended storage conditions, and produces hazardous decomposition products beneath fire situations.[9]

Side effects of metformin include metallic taste in the mouth. Symptoms may include :

diarrhea, nausea,edema, increased hunger,and a rapid heartbeat.Headaches . It can lead to anemia and reduced vitamin B12 absorption. It also leads to lactic acid. [10,11]

ANALYTICAL METHODS:

Approaches of analysis Abundant techniques, including UV, HPLC, HPTLC, LC/MS, have been described for the estimation of metformin in pharmaceutical preparation .Of these, HPLC is the most often employed method for metformin analysis. An attempt has been made to assemble all of the analytical techniques that have been utilized recently to explore metformin in this study.

UV SPECTROSCOPY TECHNIQUES:

A number of UV spectroscopy techniques have been acknowledged for the quantification of metformin hydrochloride alone and in combination with other medications. A straightforward and accurate spectrophotometric technique was devised and verified by G. Mubeen et al. for the measurement of metformin hydrochloride in both bulk and tablet format.

In an alkaline media, the amino group of metformin hydrochloride interacts with ninhydrin to create a violet-colored chromogen that can be measured spectrophotometrically at 570 nm. It followed Beer's law between 8-18 µg/ml. The drug recovery percentage for the suggested technique varied from 97-100%, showing no interference from tablet excipients[12].

Ambadas R. Rote et al. developed and validated a UV spectrophotometric method to estimate metformin hydrochloride in tablet formulations. Metformin hydrochloride is measured spectrophotometrically at 232 nm using distilled water as a solvent. It followed Beer's law within a range of 2-10 µg/ml. The medication recovery percentage for the suggested technique ranged between 102 and 105%, demonstrating that the tablet excipients had no interference.The suggested approach accurately and precisely estimates metformin hydrochloride in both bulk and pharmaceutical formulations [13].

R.H. Majithia et al. (2020) developed and validated a cost-effective Q-Absorption ratio spectrophotometric method for estimating Anagliptin with metformin hydrochloride in a synthetic combination. Anagliptin and metformin hydrochloride have an iso-absorptive point of 238 nm in pure water. The second wavelength utilized was 233 nm, which represents the λmax of metformin hydrochloride in distilled water. The drug concentration was estimated using the ratio of absorbance at the iso-absorptive point (λ1 = 238 nm) and metformin hydrochloride's λmax (λ2 = 233 nm). The technique is linear for both medications, with anagliptin ranging from 2-12 µg/mL at λ1 (r2 = 0.999) and λ2 (r2 = 0.9998), and metformin hydrochloride ranging from 5-30 µg/mL at λ1 (r2 = 0.9995) and λ2 (r2 = 0.9997).The standard addition approach yielded a recovery rate of 100.42-101.83% for anagliptin and 99.94-101.63% for metformin hydrochloride. Anagliptin's limit of detection (LOD) was 0.201 µg/mL at λ1 and 0.262 µg/mL at λ2. Metformin hydrochloride has a limit of detection (LOD) of 0.320 µg/mL at λ1 and 0.167 µg/mL at λ2. Anagliptin has a LOQ of 0.610 µg/mL at λ1 and 0.794 µg/mL at λ2. The LOQ for metformin hydrochloride was 0.972 µg/mL and 0.506 µg/mL at λ1 and λ2, respectively. The approach was found to be exact because the repeatability, interday, and intraday precision for anagliptin and metformin hydrochloride were all less than 2.00% RSD.Anagliptin plus metformin hydrochloride demonstrated improved repeatability,

interday precision, and intraday accuracy. The new approach demonstrated good application, with anagliptin and metformin hydrochloride achieving 100% assay in a synthetic mixture [14].

Madhuri Ajay Hing et al. (2016) used Q-Absorbance ratio to estimate metformin and sitagliptin levels in approved formulations. This spectroscopic approach used 237 nm (λmax of metformin) and 253.26 nm (iso absorptive point for other medications) to determine absorptivity. Both medicines exhibit linearity in concentration ranges of 5-25 µg/ml for metformin and 0.5-2.5 µg/ml for sitagliptin at 237 and 253.26 nm, respectively. QC samples were used to study accuracy, precision, and recovery across various linearity ranges. The relative standard deviation for accuracy and precision studies was found to be within acceptable limits (<2%). Metformin and sitagliptin recovery rates were 99.73-101.16% and 99.44-101.56%, respectively, confirming the correctness of the results by proposed method [15]

HIGH PERFOMANCE LIQUID CHROMATOGRAPHY:

High-performance liquid chromatography combined with M.S. L Zhang et al. presented a sensitive, specific, and selective technique for detecting metformin and rosiglitazone in human plasma [16]. The ESIC-MS/MS method was developed and validated in human plasma using phenformin as the internal standard (IS). Plasma samples were precipitated with acetonitrile and separated on a prepacked Phenomenex Luna 5u CN 100A (150 mm x 2.0 mm I.D.) column. The mobile phase was methanol:30 mM ammonium acetate pH 5.0 (80:20, v/v) supplied at 0.2 ml/min. Detection was done using a Finnigan TSQ triple-quadrupole tandem mass spectrometer with positive ion selection.

The Finnigan TSQ triple-quadrupole tandem mass spectrometer was used for detection in positive ion selected reaction monitoring (SRM) mode, using electrospray ionization. The measured ion transitions were m/z 130.27-->71.11 for metformin, m/z 358.14-->135.07 for rosiglitazone, and m/z 206.20-->105.19 for the IS. The standard curves for metformin and rosiglitazone were linear (r(2)>0.99) throughout concentration ranges of 5-3000 ng/ml and 1.5-500 ng/ml, respectively, with satisfactory accuracy and precision. Precision within and between batches was less than 15% of the relative standard deviation. Metformin and rosiglitazone had the same limit of detection (LOD) of 1 ng/ml. This method was effectively used to explore the pharmacokinetics of metformin and rosiglitazone capsules in 12 healthy Chinese volunteers. It is exact and sensitive.[16]

HIGH PERFOMANCE THIN LAYER CHROMATOGRAPHY:

A high-performance thin-layer chromatography method was developed to measure metformin hydrochloride and alpha lipoic acid, as described by Jitendra PP et al. (2020). The two medications were separated using silica gel 60F254 plates. Toluene, Ammonium Acetate (4%), and Ethyl Acetate (5:4:1 v/v/v) made up the mobile phase. It was discovered that 227 nm was the detecting wavelength. Alpha lipoic acid and metformin hydrochloride were discovered to have respective Rf values of 0.28 and 0.65. For both metformin hydrochloride and alpha lipoic acid, the technique was linear over concentration ranges of 1500–7500 ng/band and 600–3000 ng/band, respectively. The created procedure was verified in compliance with ICH regulations.

The approach was determined to be adequate, with linearity, regression value, recovery, and %RSD of intraday and interlay precision values found to be within the limits. The created HPTLC method was discovered to be straightforward, precise, and accurate[28].

Sakhare et al. (2017) investigated the stability of the high performance thin layer chromatography (HPTLC) method of examination of both the bulk medication metformin hydrochloride and the created combination formulation of benfotiamine. This method's primary goal is to use HPTLC to separate the two medications and measure their spots at 249 nm. TLC aluminum sheets of silica gel 60F 254 were used for this separation, and the mobile phase used was benzene: methanol: triethylamine (8.5:1:0.5, v/v/v).An analysis of forced deterioration

was used to determine the stability of MET and BENT. Benfotiamine and metformin hydrochloride each had a clear, distinct peak at Rf 0.72 and 0.26, respectively. For metformin hydrochloride and benfotiamine, the calibration curves were linear in the range of 500–3000 and 75–450 ng/spot, respectively. Tablet formulation underwent a series of application of the method. According to the stability research, the chromatograms of the samples that were broken down by light, dry heat, hydrogen peroxide, acid, and base revealed several extra peaks at various Rf values in addition to well-separated spots of pure metformin hydrochloride and benfotiamine. The HPTLC technique demonstrated the ability to accurately measure metformin hydrochloride and benfotiamine, even when their breakdown products from a forced degradation research were present. As a result, the approach can serve as a stability indicator [17].

A high-performance thin layer chromatographic technique for the detection of metformin, glimipride, and atorvastatin in pharmaceutical dosage form was investigated by Kumar Manikanta A et al. (2010). As the stationary phase, the technique used TLC aluminum plates precoated with silica gel 60F-254. Water, methanol, and ammonium sulphate (3.5:3.5:12.6, v/v/v) made up the solvent system. Compact spots were observed in this system for metformin, glimipride, and atorvastatin (Rf values of 0.33 ± 0.01, 0.65 ± 0.01, and 0.50 ± 0.01). Atorvastatin, glimipride, and metformin underwent densitometric analysis in the absorbance mode at 245 nm.

The calibration plots' linear regression results demonstrated a strong correlation, with atorvastatin's r2 = 0.999 ± 0.001 from 100–700 ng, glimipride's r2 = 0.998 ± 0.002 from 20–140 ng, and metformin's r2 = 0.996 ± 0.001 from 100–1500 ng, respectively. The techniques were verified in terms of recovery, toughness, accuracy, and precision. For atorvastatin, the limits of detection and quantification were 20 and 80 ng per spot; for glimipride, they were 5 and 20 ng per spot; and for metformin, they were 50 and 100 ng per spot [18].

HIGH PERFOMANCE LIQUID CHROMATOGRAPHY:

HPLC Chromatographic Methods Several high-pressure liquid chromatographic (HPLC) methods have been described for determining metformin hydrochloride alone and in combination with other drugs. Ramesh Gugulotha et al. (2016) developed and validated a reverse phase high performance liquid chromatographic (RP-HPLC) method for the detection of metformin hydrochloride (MET) in bulk and tablet dosage forms. The procedure used a Symmetry C18 column (4.6 × 150mm, 5µm) with a mobile phase of 60:40 (v/v) 50mM potassium dihydrogen orthophosphate buffer: methanol with a flow rate of 1.0 ml/min. UV detection at 262nm; MET eluted with a retention duration of 1.694 minutes.The method was continued and validated in compliance with the ICH recommendations.Validation demonstrated the method's speed, specificity, accuracy, precision, reliability, and reproducibility. The calibration curve plots were linear across the MET concentration range of 100-300 µg/mL. MET has a limit of detection (LOD) of 0.15 µg/ml and a limit of quantification (LOQ) of 0.5 µg/mL [19].

Nilesh Nikam et al. (2019) established a simple and reproducible method for measuring Metformin (MET) using Reverse Phase High Performance Liquid Chromatography (RP-HPLC).

Metformin was separated on a C18 column (4.6x250 mm, particle size 5µm) with a pH of 3.0 phosphate buffer and methanol, detected at 238nm using UV. The mobile phase was an isocratic elution of phosphate buffer with a pH of 3.0 and methanol, with varying ratios and flow rates. The final ratio was 30:70 v/v phosphate buffer with a pH of 3.0 and a flow rate of 1mL/min. The suggested approach for quality control analysis of metformin is suitable, as it meets statistical validation factors such as linearity, accuracy, precision, and inter-day and intra-day variation (98%-102%) [20].

REVERSE PHASE HIGH PERFOMANCE LIQUID CHROMATOGRAPHY:

Reverse- Phase Umatheet al[21] devised a simple reverse phase high-performance liquid chromatography method for detecting metformin levels in rat plasma. The method used a C18 column (300 mm × 2.4 mm i.d.), ammonium acetate (0.15 M), and acetonitrile (90:10; pH-5.5; 1.0 ml/min) as the mobile phase, with UV detection at 236 nm. Acetonitrile was also used to deproteinize rat plasma and extract metformin. The assay was linear from 0.33 µg to 16.6 µg/ml with a correlation coefficient of 0.994 and a retention period of 4.7 min. The approach was exact (% CV < 15%), accurate, and appropriate for studying the pharmacokinetics of orally given metformin in rats.Using a C18 analytical reverse phase column, the reverse phase high performance chromatography method was developed to quantify metformin hydrochloride in pharmaceutical formulations and raw materials.

Saeed et al. developed and validated this method for the analysis of metformin [22]. There was an internal standard that was Diazepam. The method was linear over the concentration range of 0.312-5 mug/ml (R2=0.9995). The mobile phase was composed of methanol-water (30:70v/v), pumped at a flow rate of 0.5 ml/min and the retention period was approximately 4.4min. The method was detected by UV absorbance at 233 nm. Metformin had a detection limit of 0.1 mug/ml and a quantitation limit of 0.3 mug/ml.

The method's sensitivity and reproducibility make it suitable for the quantitative analysis of metformin in neodipar tablets. The findings obtained were good, and the method is fast, accurate, economical, and selective.[22]

ADVANTAGES AND DRAWBACKS:

The use of HPLC in environmental analysis is frequently hampered by issues that do not arise in other analytical fields. The components that are being identified are typically in sample matrices that can produce a lot of interference, and they are typically at parts per million levels or less. The primary needs for an HPLC system are column efficiency and the sensitivity and selectivity of the detection system in order to design successful methodologies.

It is no coincidence that HPLC is the most widely used analytical technique. The main benefit is that it may be used to a wide range of analytes, including big biomolecules and polymers as well as small organic compounds and ions. HPLC gained an matchless advantage as "the perfect analytical tool" when it successfully coupled with MS, which offers unparalleled sensitivity and specificity. For bio analytical testing (drugs in biological fluids), trace analysis for residues in food, forensic and environmental materials, and life science research, HPLC–MS is hurriedly taking the place of conventional platform technology [9,21,22,29]

ESTIMATION OF METFORMIN HYDROCHLORIDE DRUG WITH DIFFERENT TECHNIQUES:

Table.1

AUTHOR	DESCRIPTION	REFERENCE
Karim *et,al* 2012 **(SPECTROPHOTOMETRY)** **(Metformin HCL)**	Concentration range- 1-25µg/ml Wavelength- 233nm % Recovery-98% to 102% Limit of detection and limit of quantification LOQ-0.6745 µg/ml LOD-0.2226 µg/ml Flow rate-1.0mL/min	**[23]**
Nief *et,al* 2012 **(SPECTROPHOTOMETRY)** **(Metformin HCL and Oxidative coupling reaction with 1-naphthol)**	Concentration range- 2-20µg/ml Wavelength- 580nm % Recovery-99.75% to 100.25% Relative standard deviation –better than 1% Molar absorptivity-3.66×10^4 1/mol.cm	**[24]**
Raniah Q Gabr *et,al* 2010 **(HPLC)** **(Metformin In Human Plasma And Urine)**	Column- C18(250mm×4.6mm× 5µm) Mobile phase- Acetonitrile: KH_2PO_4 (34:66%v/v) and Sodium Dodecyl Sulphate And Sodium Dodecyl Sulphate Mm Isocratic Mode Flow rate -0.7mL/min Wavelength- 236nm Retention time - 4.33 min	**[25]**
Mrs.Sheena Moncy *et,al* 2014 **(RP-HPLC)**	Column-PHENOMEX Luna C18(150mm× 4.6mm× 5µm)	**[26]**

(Linagliptin and Metformin)	Mobile phase- Phosphate buffer:Methanol:Acetonitrile: (65:10:25%v/v) Flow rate-1.0mL/min Retention Time- Metformin :2.2min Linagliptin:7.8min Wavelength-231nm LOD and LOQ -2.64µg / ml and 6.9µg / ml for Linagliptin and 3.08 µg / ml and 9.3µg / ml for Metformin respectively	
Ebru. U *et,al* 2013 **(GC_MS)** **(Metformin)**	Derivatization of Metformin was achieved by N-methyl bis (trifluoroacetsamide) Concentration range- 100-300ng/ml % Recovery-94.39% to 97.57% LOD and LOQ -40 ng/mL and 100 ng/mL respectively.	**[27]**

REPORTED METHOD FOR METFORMIN- HPLC, UV SPECTROSCOPY

Table.2

AUTHOR	DESCRIPTION	REFERENCE
W. Abu dayyih *et,al* 2018 **(RP-HPLC)** **(Vildagliptin And Metformin HCL)**	Column- Xterra C18 column (250 mm×4.6 mm I.D × 5µ) Mobile phase-Acetonitrile: Phosphate buffer (pH 6.0): water (65: 20:15v/v/v) Flow rate - 1mL/min Wavelength- 239nm	**[35]**
A.S.K Sankar *et,al* 2013 **(RP-HPLC)** **(Sitagliptin+ Metformin)**	Column-PHENOMENEX Luna C18(250mm× 4.6mm× 5µm) Mobile phase-Potassium dihydrogen phosphate : Acetonitrile (60:40%v/v) Flow rate-1mL/min Retention time – 2.718 min Wavelength-252nm	**[36]**
Balamurugan Krishnan *et,al* 2020 **(RP-HPLC)** **(Sitagliptin + Metformin)**	Column- Monolithic C18(100mm×4.6mm× 5µm) Mobile phase- Acetonitrile: Methanol(50:50%v/v) Flow rate -0.3-0.5mL/min Wavelength-210nm Retention time - 4.33 min	**[37]**
Usharani Gundala *et,al* 2013 **(UV Spectrophotometry)** **(Vildagliptin and Metformin)**	Retention time- 0.859min Wavelength-217 & 234nm The % recovery -98- 102%	**[38]**

	LOD and LOQ -0.023 µg / ml and 0.225 µg / ml for Vildagliptin and 0.44 µg / ml and 1.35 µg / ml for Metformin respectively	
Dr. Osman Ahmed *et,al* 2019 **(Stability Indicating)** **(Sitagliptin + Metformin)**	Column- Persil C18 (250mm×4.6mm× 5µm) Mobile phase- Octane sulphonic acid buffer: acetonitrile (35:65 %v/v) Flow rate-1.0mL/min Wavelength-260nm % degradation (Basic) – 9.25%	**[39]**

IMPURITIES PROFILING STUDY : DRUGS AND THEIR IMPURITIES

1) METFORMIN HYDROCHLORIDE AND TENELIGLIPTIN HYDROBROMIDE HYDRATE

V. N. Ghodke et al. Author has been declared that in his research article To detect the presence of impurities in the tablets of metformin hydrochloride and teneligliptin hydrobromide hydrate, a reliable, accurate, and exact analytical technique was created. Better impurity separation was achieved by optimising the gradient using a BDS Hypersil C18 250×4.6 mm, 5µ column that was operated at 35 °C. Acetonitrile was utilised as mobile phase B, whilst octane sulfonic acid and phosphate buffer with triethylamine at pH 3.0 were utilised as mobile phase A. A 1.0 mL/min pump was used to move the mobile phase. At 210 nm, the chromatogram was observed, and the gradient was adjusted for improved resolution. Findings: The percentage of metformin HCL and teneligliptin recovered from the LOQ level to 150% was more than 90%.

Metformin HCl, teneligliptin, melamine, cyanocobalamin, and teneligliptin impurity A had correlation coefficients of 0.999 and 0.998, respectively, with r 2. According to the robustness research, the technique was unaffected by changes in method variance. Maximum degradation was seen with peroxide during the stress trial involving acid, base, peroxide, and temperature, demonstrating the molecule's susceptibility to oxidative stress. Conclusions: The developed method can be used regularly for the related substance analysis of metformin hydrochloride and teneligliptin hydrobromide hydrate tablets in the quality control laboratory at the manufacturing site during the commercial manufacturing process because it is precise, accurate, robust, and linear.[30]

2) METFORMIN

Gabriela klaczkow et al. Author has been declared that in his research article This study's goal was to introduce a high-performance liquid chromatography (HPLC) technique that can be used to detect and measure contaminants in pharmaceutical products that include solely met-formin hydrochloride as an active ingredient. One biguanide derivative that becomes active after oral dosing is metformin (dimethylbiguanide). When insulin secretion is partially maintained in patients with type II diabetes (insulin-independent), it lowers their basic and postprandial blood glucose levels. A spectrophotometric detector (λ = 218 nm) and a PAR-TISPHER SCX column were used to separate the contaminants. The mobile phase consisted of a 1.7% (w/v) ammonium dihydrogen phosphate water solution, with 85% orthophosphoric acid added to bring the pH down to 3.1.

Since the suggested method is quick, sensitive, and selective, it can be used to assess medicinal items for which only cyanoguanidine or cyanoguanidine and melamine assays are now conducted, as well as those for which impurity tests are not currently conducted.[31]

3) GLIMEPIRIDE AND METFORMIN HYDROCHLORIDE

Shraddha Pawar et al. Author has been declared that in his research article We developed a gradient approach to quantify impurities of glimepiride and metformin hydrochloride in combination pharmaceutical dosage forms. The method uses high-performance liquid chromatography (HPLC) on a Waters Symmetry -C8.5µ 4.6 x 250mm column at 50°C. It uses a mobile phase of pentane sulfonic acid sodium salt buffer pH 3.5 and acetonitrile to detect known and unknown impurities in glimepiride and metformin hydrochloride tablets. The approach effectively distinguishes between glimepiride sulfonamide (GS), glimepiride urethane (GU), glimepiride 3-isomer (GI), metformin related chemical A (MA), glimeiride (G), metformin hydrochloride (M), and unknown contaminants in the formulation.

Quantifying all components involves using a gradient algorithm with UV detection at 230nm. The method is validated for specificity, linearity, and range for GS, GU, GI, MA, M, and G, as well as accuracy with spiked impurities (80%-120% of the required limit), precision, and robustness. The limits of quantification are 1.50 µg mL-1 for M, 0.10 µg mL-1 for G, 0.30 µg mL-1 for MA, 0.24 µg mL-1 for GS, 0.10 µg mL-1 for GU, and 0.22 µg mL-1 for GI. The suggested approach accurately detects and quantifies contaminants in M and G tablets without interference from excipients.[32]

4) VILDAGLIPTIN AND METFORMIN HCL

B. D. Musmade et al Author has been declared that in his research article The quantitative evaluation of associated impurities of Vildagliptin and Metformin HCL from combination tablet dosage form was accomplished using a precise, accurate, and reliable method. The methanol and buffer mixture in a 95:5 ratio served as mobile phase B, while the ammonium dihydrogen orthophosphate and octane sulfonic acid sodium salt buffer mixture at pH 4 served as mobile phase A. The mobile phase was pumped over a BDS Hypersil C8, 250 x 4.6 mm, 5µ, HPLC column that was kept at 35°C at a flow rate of 0.8 ml/minute. A 10µl injection volume was used for all solutions, and the chromatograms were seen at 210 nm in accordance with the best possible response of the analytes and contaminants.The percentage of Metformin HCL recovered was 90.4, 92.3, 99.4, and 99.2%, but the percentages of Vildagliptin recovered from LOQ, 50, 100, and 150 percent, respectively, were 90.5, 94.5, 99.6, and 98.3%. With correlation coefficients (r2) of 0.998 for Vildagliptin and Metformin HCL, the technique was found to be linear from LOQ to 150%. The method is both robust and specific because there was no discernible interference from diluent and placebo during the retention time of all known impurities and principle analytes in the specificity study, and no discernible changes in the chromatographic pattern for standard, system suitability criteria, and sample chromatograms during the robustness study. The technique can be applied to the pharmaceutical industry's quality control labs to analyse linked compounds from these combination medication items.[33]

5) METFORMIN HCL AND CANAGLIFLOZIN

Patel S et al. Author has been declared that in his research article.For the measurement of associated impurities of metformin HCl and canagliflozin in combination tablets, a straightforward, affordable, selective, and accurate RP-HPLC approach has been created and validated. On a Hypersil BDS C18 column (250 mm x 4.6 mm, 5 µm), the RP-HPLC method with gradient elution analysis was carried out using a mobile phase consisting of 0.05M potassium phosphate buffer pH-5.0 and acetonitrile in a 70:30 v/v ratio at a flow rate of 1.0 ml/min. The detection wavelength was 290 nm. The ICH requirements are followed in the validation of the analytical method.A. For canagliflozin and its associated impurity 2, linearity was also noted in the LOQ-7.5µg/ml range. For every analyte, the correlation coefficient was found to be less than 0.99. The recovery percentage for Metformin HCl Impurity

A was determined to be 98.128% at the lowest and 101.996% at the highest. Similarly, for Canagliflozin Impurity 2, the recovery value was determined to be at least 98.472% and as high as 101.150%. The percentage recovery values for Canagliflozin Impurity 2 ranged from 98.472% to 101.150%, while those for Metformin Impurity A ranged from 98.128% to 101.996%. The LOD values for metformin HCl and its associated impurity A were determined to be 0.495µg/ml and 0.098µg/ml, respectively. The LOD values for Canagliflozin and its associated Impurity 2 were determined to be 0.248µg/ml and 0.050µg/ml, respectively. 1.500µg/ml was the LOQ value discovered forFor canagliflozin, the LOD value was 0.248 µg/ml, while for its associated impurity 2, it was 0.050 µg/ml. The LOQ values for metformin HCl and its associated impurity A were determined to be 1.500µg/ml and 0.297µg/ml, respectively. For canagliflozin, the LOQ value was determined to be 0.753µg/ml, while for its associated impurity 2, it was 0.151µg/ml. The findings demonstrate the accuracy, precision, simplicity, and speed of the developed method.[34]

CONCLUSION:

This study covers a variety of techniques for estimating metformin hydrochloride for pharmaceutical manufacture, including a wide range of instrumental techniques and also studying the impurities of metformin.. The majority of these techniques are labor-intensive and sophisticated. Metformin hydrochloride can be determined using any of the following instrumental methods: they are simple, accurate, sensitive, have a low detection limit, quick to analyze, and cost-effective.The most advanced analytical techniques currently available for MET determination are highlighted in this review. To sum up, a variety of methods are available for MET analysis in pharmaceutical formulations and biological materials.

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