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Review Article

An overview on analytical estimation of ertugliflozin

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ABSTRACT

Ertugliflozin is a medicine that is used to treat type 2 diabetes. It's given as a solo medication or in a fixed-dose combination with sitagliptin or metformin. Ertugliflozin belongs to the gliflozin class of medications and is a sodium/glucose cotransporter 2 (SGLT2) inhibitor. In the already available literature, various analytical and bioanalytical methods are feasible. The two aspects of the analytical methods covered here are spectroscopy and chromatography. Advanced analytical techniques such as 3D fluorescence spectroscopy, HPLC, HILIC, and UPLC MS/MS were used to examine Ertugliflozin in pure, dosage forms, and a variety of biological matrixes. This paper undoubtedly beneficial in future for the researchers who are working in development and validation of various analytical methods for quantification of Ertugliflozin form its bulk and pharmaceutical dosage form.

Keywords: Ertugliflozin, UPLC MS/MS, HILIC, SGLT2 inhibitors, Analytical and bioanalytical techniques

INTRODUCTION

Around 463 million individuals worldwide have type 2 diabetes mellitus [1], which is characterised by polydipsia, polyuria, and polyphagia and necessitates lifelong antidiabetic therapy [2]. The treatment objectives include achieving glycemic control and lowering diabetes-related cardiovascular risk. Metformin, an insulin sensitizer, is used to treat patients who have recently developed diabetes. Metformin has a low risk of hypoglycemia and fewer drug interactions, making it a very safe and acceptable first-line medicine for the treatment of early type 2 diabetes mellitus [3]. The pathophysiology of type 2 diabetes mellitus is multifactorial, involving several organs, and treatment with a cocktail of medications with distinct modes of action effectively lowers plasma glucose levels [4]. Inhibition of the sodium glucose co-transporter type 2 (SGLT-2) is a new therapy option for type 2 diabetes mellitus. These drugs work by blocking the SGLT-2 transporter in the kidneys, which promotes glucose excretion in the urine and lowers plasma glucose levels [5].

Chemistry: Ertugliflozin is a medication that is used to treat type 2 diabetes. It's an inhibitor of the sodium glucose co-transporter 2 (SGLT2). SGLT2 inhibitors reduce fasting and postprandial blood glucose levels by decreasing renal glucose reabsorption and increasing urine glucose

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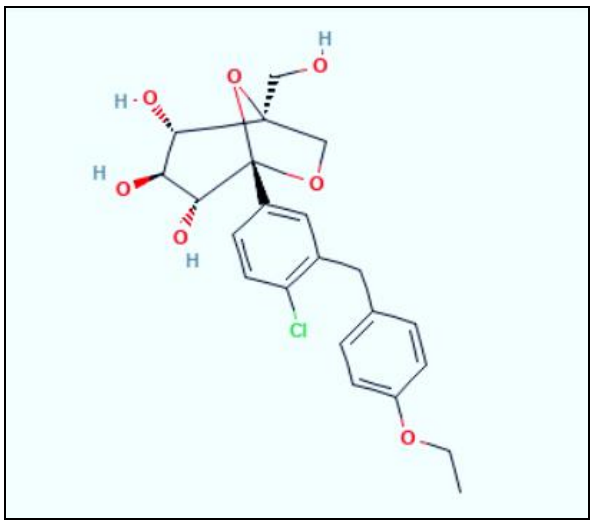
excretion. IUPAC Name of ertugliflozin is (1S,2S,3S,4R,5S)-5-[4- chloro-3-[(4-ethoxyphenyl) methyl] phenyl]-1- (hydroxymethyl)-6,8-dioxabicyclo [3.2.1] octane-2,3,4- triol
Molecular formula: C22H25ClO7
Molecular weight:436.9 Daltons.[5]



Molecular Structure of ertugliflozin

It's a white powder that's soluble in ethanol and acetone, but only marginally soluble in ethyl acetate and acetonitrile, and only sparingly soluble in water. It's available as a single medicine as well as in a combination with Sitagliptin and metformin hydrochloride. Few bioanalytical, analytical technique development and validation, and stability suggesting investigations are accessible with the drug (ertugliflozin) and also with the combination of Sitagliptin and metformin, according to the collection of papers. [6]

Pharmacodynamic:
The drug ertugliflozin causes a negative balance and osmotic diuresis by increasing urine glucose excretion. As a result, diabetes patients' body weight and blood pressure have been observed to be dramatically reduced by this antidiabetic medication.

a) **Absorption:**
Preclinical investigations revealed that ertugliflozin is well absorbed, with a 70-90 percent oral bioavailability. Tmax was observed to occur 0.5-1.5 hours after dosing. The Cmax and AUC after oral treatment appeared to be dosage proportionate. Cmax and AUC were 268 ng/ml and 1193 ng h/ml, respectively, after 15 mg administration.

b) **Volume of Distribution:** The apparent volume of distribution of ertugliflozin after oral dosing was observed to be 215.3 L. After intravenous administration of ertugliflozin, the steady-state volume of distribution is 85.53 L.

c) **Protein Binding:** Ertugliflozin binds to plasma proteins in a high-binding range of 94-96 percent, regardless of the supplied concentration.

d) **Metabolism:** Monohydroxylation, O-demethylation, and glucuronidation reactions define the metabolic profile of ertugliflozin in liver microsomes and hepatocytes, according to in vitro investigations. Eight distinct metabolites identified in plasma, faeces, and urine are thought to be involved in the metabolism of ertugliflozin. The unaltered form of ertugliflozin was found to make up the majority of the administered dosage in plasma. In addition, six minor metabolites were discovered in circulating plasma. Ertugliflozin was recovered in 91 percent of cases, with 50 percent of the drug ending up in the urine and 41 percent ending up in the faeces. Approximately 168 hours after the initial injection, the provided dose was recovered. Urine clearance was quite rapid, and after 24 hours, 80 percent of the dosage was recovered in urine. The ertugliflozin dose that was removed in urine was made up of seven major metabolites and the unaltered ertugliflozin as a minor metabolite. The elimination rate in faeces varied based on the patient's bowel movements, however after 168 hours of initial administration, 98.5 percent of the dose was eliminated in faeces. Unchanged ertugliflozin and three other minor metabolites made up the majority of the eliminated dosage.

Mechanism of action: The glucose from the blood is filtered for excretion and reabsorbed in the glomerulus as part of the regular process, thus less than one percent of this glucose is expelled in the urine. Reabsorption is handled by the sodium-dependent glucose cotransporter (SGLT), primarily type 2, which accounts for 90% of reabsorbed glucose. Ertugliflozin is a modest SGLT2 inhibitor that enhances glucose excretion while lowering hyperglycemia without requiring excessive insulin secretion.
Half Life: The terminal elimination half-life of ertugliflozin is 11-17 hours [7-10]

Validation of RP-HPLC method:
Theoreticians (researchers) and practical analyzers alike are interested in method development and optimization in liquid chromatography. “Efforts in separation, such as optimised column, mobile

phase, and optimal detection wavelength, can make a world of difference when establishing HPLC methods for routine analysis. Validation is defined as "recorded evidence that a process, system, or facility will consistently generate a product that meets its planned requirements and quality features."

Method Validation: The process of establishing that an analytical method is suitable for its intended purpose is known as method validation. The United States Pharmacopoeia (USP), the International Conference on Harmonization (ICH), the World Health Organization (WHO), and the Food and Drug Administration (FDA) provide a framework for completing such validations for pharmaceutical techniques.

Parameters for Method Validation:
The parameters for method validation as defined by ICH (International Conference on Harmonization) guidelines are summarized below:

- **Accuracy**

The closeness of agreement between the values, which is acknowledged either as a conventional true value or an approved reference value found, is expressed by the accuracy of an analytical technique. The accuracy studies' results are provided as a percentage recovery (the results must be followed within a range of 98–102%).

- **Precision:** The degree of dispersion (closeness of agreement) between a set of measurements acquired from multiple sampling of the same homogeneous sample under the stipulated conditions is expressed by the precision of an analytical method. It's usually represented as a percentage of the standard deviation.

Precision may be considered at three levels:

I. **Repeatability:** Over a short period of time, expresses the precision under the same operating conditions. Intra-assay precision (Relative Standard) is another name for it. Repeatability studies must have a variance of less than 2%.
II. **Intermediate Precision:** Expresses the precision within laboratory variability, such as various days, different analysts, different equipment, reagents, and so on. (Intermediate precision studies must have a relative standard deviation of less than 2%).
III. **Reproducibility:** Describes the degree of precision between laboratories (collaborative studies, usually applied for standardisation of methodology).

- **Specificity:** The ability to assess the analyte definitively in the presence of components that may be present is known as specificity. Impurities, degradants, matrix, and other substances are examples of these.

- **Linearity**: The capacity of an analytical process to produce test results that are directly proportional to the concentration of analyte in the sample (within a certain range) is known as linearity (the correlation coefficient for linearity studies must be r>0.999).

- **Range**: The difference between the sample's upper and lower analyte concentrations for which the analytical technique has been proved to have a reasonable degree of precision, accuracy, and linearity is the range of an analytical procedure.

- **Robustness:** Robustness is a measure of an analytical technique's ability to remain unaffected by modest but deliberate changes in system characteristics, and it demonstrates its dependability in regular use.

- **Ruggedness**: An analytical technique's robustness/ruggedness is a measure of its capacity to remain unaffected by modest but deliberate changes in process parameters, and it reflects its dependability in routine use. [11-15]

- **Limit of Detection**: The lowest amount of analyte in a sample that can be detected but not necessarily quantified as an exact number is the detection limit of an individual analytical method. The Limit of Detection (LOD) is a concentration at a given signal-to-noise ratio. The injected amount in chromatography that results in a peak with a height at least twice or three times that of the baseline noise level is known as the detection limit.

S/N=2/1 or 3/1
Where, S= Signal, and N= Noise.
It may be calculated based on standard deviation (SD) of the response and slope of the curve(S):
LOD= 3.3(SD)/S Where,
SD= Standard deviation, and S= Slope.

- **Limit of Quantitation**: The lowest amount of analyte in a sample that can be quantitatively measured with sufficient precision and accuracy is the quantitation limit of a particular analytical process. The Limit of Quantitation (LOQ) is a concentration at a given signal-to-

noise ratio. The quantitation limit in chromatography is the injected amount that produces a peak with a height ten times that of the baseline noise level.

S/N=10/1

Where, S= Signal, and N=Noise.

It may be calculated based on Standard Deviation (SD) of the response and slope of the curve(S).

LOQ=10 (SD)/S

Where, SD= Standard deviation, and S= Slope.

China Babu et al. developed and validated a stress-indicating RP-HPLC technique for simultaneous quantification of Ertugliflozin and Sitagliptin in bulk and formulation. The experiment was carried out in a Waters HPLC with a c18 column capacitate (250X4.6 mm, 5 m particle size) (Waters). The mobile phase was composed of 0.5mM potassium dihydrogen orthophosphate (buffer) Ph 5.3 and methanol (55:45) v/v peak elution of ertugliflozin at 2.3 min and Sitagliptin at 4.6 min. For Ertugliflozin and Sitagliptin, the LOD and LOQ values were found to be 0.3g/ml and 0.1g/ml, respectively. They also design a stress suggesting investigations in RP HPLC technique mobile phase as 0.75mM di hydrogen orthophosphate buffer at pH 8.5 and acetonitrile in a 60:40 v/v PDA detector was used and the detection was carried out at 263nm with a flow rate of 1.5ml/min. System appropriateness, specificity, precision, linearity, accuracy, LOD& LOQ, and robustness are among the validation parameters. Ertugliflozin and Sitagliptin were reported to have linearity of 0.9998 and 0.9996, respectively. Ertugliflozin and Sitagliptin have theoretical plates of 3985 and 6425, respectively. Ertugliflozin and Sitagliptin had accuracy mean percent recovery of 99.90 and 100.91, respectively. Changes in flow rate, temperature, and mobile phase composition were used to test the method's resilience. [16]

Nizami et al. used an RP-HPLC approach to develop and evaluate an analytical method for simultaneous quantification of Ertugliflozin and Metformin in tablet dose form. The experiment was carried out on a Waters HPLC with a c18 column (150 mm x 4.6 mmd, 5 m) (Waters), a mobile phase of potassium dihydrogen ortho phosphate: acetonitrile (70:30v/v), and a flow rate of 1 ml/min. The discovery took place at 240nm using a PDA detector. Ertugliflozin had a retention time of 3.2 minutes, while Metformin had a retention duration of 2.1 minutes. They validated metrics including linearity, accuracy, precision, selectivity, LOD&LOQ, and so on using this method. Ertugliflozin and metformin's theoretical plates are 4435 and 44304, respectively. According to the ICH, the validation parameters for ertugliflozin and metformin are linearity throughout a range of 1.5-4.5g/mL and 100-300g/mL, respectively. Metformin had a percentage recovery of 99.889 percent to 99.631 percent, while Ertugliflozin had a percentage recovery of 100.181 percent to 100.814 percent. For Ertugliflozin and Metformin, the LOD and LOQ values were found to be 0.43g/ml and 1.30g/ml, respectively. [17]

Harshalatha P, et al. established a new RP-HPLC method for determining Ertugliflozin and Sitagliptin in bulk and tablet dosage forms simultaneously. The experiment was carried out in a Waters HPLC column with a c18(250 mm X 4.6 mm; 5m) column and a mobile phase of 0.2 percent orthophosphoricacid and acetonitrile (60:40) v/v. The flow rate was set to 1 mL/min, and the detection was done with a photo diode array detector operating at 250nm for a total of 6 minutes. Ertugliflozin and Sitagliptin have peak elution times of 2.3 and 3.9 minutes, respectively. Selectivity, linearity, limit of detection, limit of quantification, robustness, precision, sensitivity, accuracy and a range of other validation factors are listed by the ICH. The theoretical plate numbers for Ertugliflozin and Sitagliptin are 8496 and 64825, respectively. At concentrations of 32.50 – 97.50 g/ml and 216.50 – 649.50 g/ml, respectively, ertugliflozin and Sitagliptin were shown to be linear. The samples were analysed at three different concentrations of 50, 100, and 150 percent for the recovery investigation. Changes in column temperature, flow rate, and mobile phase pH were used to test robustness. [18]

For the simultaneous measurement of Sitagliptin and ertugliflozin in bulk and tablet dosage forms, **Amtul Hadi Hadiya and Mohammad Yunoos** established a new verified stability indicating RP-HPLC method. The chromatographic separation was performed on an Agilent ODS C18 (4.6 x 150 mm, 5 particle size) column with a mobile phase of 50:50 percent v/v acetonitrile: phosphate buffer (adjusted to pH 5.4 with 0.1 percent ortho phosphoric acid) at 1.0 ml/min. The analyte was monitored using a UV detector with a wave length of 215nm and a runtime of 10 minutes, with peak elution times of 2.4 and 4.5 minutes for ertugliflozin and Sitagliptin, respectively. Ertugliflozin's theoretical plates were determined to be 3493, whereas sitagliptin's were found to be 4706. According to ICH criteria, the approach was validated. Sitagliptin's linearity range was 25-125 g/ml, while Ertugliflozin's was 3.75-22.5 g/ml. The percent recovery of accuracy was proved using the standard addition method at three distinct concentrations of 50%, 100%, and 150 percent. Deliberate variations in flow rate, mobile organic phase, and temperature were used to determine robustness. Stress tests were carried out. [19]

P.V. Rao and colleagues established a new stability-indicating RP-HPLC method for estimating ertugliflozin and Sitagliptin in bulk and pharmaceutical dose forms. The separation took place in the Agilent column (1504.6, 5m) dimensions, and the experiment was carried out in HPLC (Waters). The buffer (Potassium di hydrogen Ortho Phosphate): Acetonitrile (70:30 V/V) is used in the mobile phase. The flow rate remained constant at 1.0 ml/min. The Photo Diode Array detector effluent was monitored at 240 nm for 3.2 minutes (Ertugliflozin) and 2.106 minutes (Sitagliptin). As a diluent, acetonitrile and water in a 50:50 ratio were utilised. The method was validated according to ICH recommendations, and Ertugliflozin and Sitagliptin linearity was determined to be 3.75-22.5g/ml and 25-0.150g/ml, respectively. The mean recovery of Ertugliflozin and Sitagliptin was computed and 1002 percent acceptable. Changes in flow rate, column temperature, and mobile phase composition all contribute to robustness (Acetonitrile proportion). Degradation tests were carried out. [20]

Venkateswara Rao et al., For the simultaneous assessment of metformin hydro chloride and ertugliflozin bulk and pharmaceutical dose form, a new stability indicating reverse phase HPLC method was designed and validated. The separation took place in column BDSc8 (150mm4.6mm5mm) and the mobile phase was made of buffer: acetonitrile (55:45v/v) in a Waters HPLC. The flow rate was kept constant at 10 mL/min, and detection was done with a light diode array (PDA). Metformin had a retention time of 2.33 ml/min while Ertugliflozin had a retention time of 3.136 ml/min. System appropriateness, linearity, precision, accuracy, robustness, LOD, and LOD were the validation parameters for this experiment. Metformin and Ertugliflozin had linearity values of 125-170 mg/ml and 1.875-11.25 mg/ml, respectively. Metformin's LOD and LOD were 1.70mg/ml- 5.16mg/ml, while Ertugliflozin's LOD and LOD were 0.07mg/ml-0.21 mg/ml. Metformin had an accuracy score of 99.13 percent -101.63% and Ertugliflozin had an accuracy rating of 99.05 percent - 101.10 percent. Changes in oven temperature (50 c), mobile phase composition, and flow rate (0.1 ml/min) were used to determine robustness. [20]

For the measurement of ertugliflozin and Sitagliptin in rat plasma, **Xiangjun Qiu et al.** developed a UPLC MS/MS technique. The experiment was carried out using a UPLC MS/MS system, with separation taking place on a BEH c18 column (2.1mm 50mm 1.7mm) with a mobile phase of acetonitrile and water with o.1% formic acid by gradient elution. Multiple reaction monitoring (MRM) in positive electrospray ionisation was used to detect Ertugliflozin using the m/z 437.2-329.0 transition for quantification and the m/z 437.2-207.5 transition for qualification, and Sitagliptin using the m/z 408.2-235.0 transition for quantification and the m/z 408.2-174.0 transition for qualification. Ertugliflozin concentrations ranged from 1 to 1000 mg/ml, while Sitagliptin concentrations ranged from 2 to 2500 mg/ml, indicating that the approach is linear. Precision values ranged from 1.6 to 10.9 percent intraday and 0.8-13.3 percent interday for both medicines, with accuracy values ranging from 15.7 to 14.6 percent. The flow rate was set to 0.4 ml/min and the run time was set to 3 minutes. Multiple reaction monitoring (MRM) mode was used to quantify ertugliflozin, sitagliptin, and IS, with transitions of m/z 437.2329.0 and 437.2207.5 for ertugliflozin, m/z 408.2235.0 and m/z 408.2174.0 for sitagliptin, and m/z 285.0154.0 for IS, respectively. Masslynx 4.1 software was used to collect data and control the instrument. [21]

Yali Liang et al., studied effect of food on the pharmacokinetics of Ertugliflozin and its fixed dosage combinations (Ertugliflozin /Sitagliptin and Ertugliflozin/ metformin) was done in the Waters atlantis HILIC and separation take place in the column (3mmx2.1×50mm)mobile phase was composed of acetonitrile: water (80:20 v/v) containing 10 ml ammonium acetate (pH4.7) and detection was performed by sciex API4000 in the positive ion mode and MRM values for Sitagliptin was m/z 408-235 and metformin for 130-71 and plasma concentrations was determined based on the pharmacokinetics parameters like AUC, Cmax, Tmax. Metformin had a Tmax of 2.3 hours (fasted) and 4.0 hours (fed), while Sitagliptin had a Tmax of 3.0 hours (fasted) and 1.8 hours (fed) (fed). Ertugliflozin's AUC was within the bioequivalence range of 80 to 125 percent, while metformin's Cmax reduced to 29 percent in the fed state and Sitagliptin's was 90 percent. [22]

M.Anjali, et al., Using the Simultaneous Equation Technique, we designed and validated a UV method for Ertugliflozin and Sitagliptin. The experiment was carried out in a UV spectrophotometer (PG instruments). This method relies on the measurement of absorbance at two wavelengths, 210 nm and 221 nm, to solve simultaneous equations. As a diluent, a 1:1 v/v mixture of HPLC grade water and acetonitrile was sonicated for 15 minutes. The UV range 200–400 nm was used to scan the working solutions of both medicines. Both medications' overlay spectra were recorded. The wavelengths 210 nm (for STG) and 221 nm (for ETR) were chosen for simultaneous equation analysis of both medicines (210 nm for Sitagliptin and 221 nm for Ertugliflozin). According to ICH criteria, the approach was

validated. The percent RSD was determined to be less than 2%, and the specificity, precision, and ruggedness were all estimated. The method's robustness was tested by adjusting the wavelength by 2 nm. The obtained percent RSD was less than 2%. [23]

Laxmi et al. devised an RP-HPLC method for estimating Ertugliflozin and Sitagliptin in bulk and tablet dose forms simultaneously. The separation takes place in a C18 column (250mm 4.6mm I.D., 5m) with 0.1M dipotassium hydrogen phosphate and methanol (65:35) v/v as the mobile phase. Ertugliflozin elution peaked at 3.02 minutes, with a run time of 7 minutes, and was detected by a PDA detector at 225nm wavelength, with a flow rate of 1 ml/min and a pH of 3.5. According to ICH criteria, the approach was validated. In the range of 50–150g/ml for Sitagliptin and 7.5–22.50g/ml for ertugliflozin, the association was shown to be linear. Minor adjustments in the flow rate of the mobile phase (0.1 ml/min), pH, detection, mobile phase ratio, and column temperature (2°C) were used to test the method's resilience. The LOD and LOQ were determined to be 0.071 and 0.237 g/ml, respectively. [24]

D.G. Han et al. devised an HPLC method for determining ertugliflozin in rat plasma that included fluorescence detection. They presented a new bioanalytical approach that combined high-performance liquid chromatography (HPLC) with fluorescence detection. The separation was carried out using a Kinetex C18 column (250 4.6 mm, 5 m, 100; Phenomenex, Torrance, CA, USA) with an isocratic mobile phase of acetonitrile and 10 mM potassium phosphate buffer, protected by a C18 guard column (pH 6.0). A flow rate of 1 mL/min is used. The injection volume was 20L, with a total run time of 20 minutes. A fluorescence detector recognised the peak at an optimum excitation and emission wavelength pair of 277&320nm, respectively. According to ICH criteria, the approach was validated. Calibration curves (n = 5) were created by applying linear regression analysis to plot the peak area ratios of ERTU to IS (y-axis) vs the concentration ratios of ERTU (4–2000ng/mL) to IS (1000ng/mL) in plasma (x-axis). [25]

A Lakshmana Rao and U Krishnaveni devised a stability-indicating RP-HPLC method for estimating metformin and ertugliflozin simultaneously. The Waters HPLC 2695 was used to analyse the medicines. On a Denali C18 (150 x 4.6mm, 5m) column, isocratic separation was obtained with a mobile phase of 0.01 N KH2 PO4: acetonitrile (60:40 V/V), pH adjusted to 5.4 with 0.01 percent orthophosphoric acid. The flow rate was held constant at 1 mL/min, and analytes were detected using a UV detector set at 224 nm with a 6 minute run period. Ertugliflozin and metformin have peak elution times of 3.20 and 2.35 minutes, respectively. The sample injector volume was 20L, and the analysis was performed at room temperature. According to ICH criteria, the approach was validated. Metformin and ertugliflozin had theoretical plates of 5675 and 7593, respectively. Metformin linearity concentrations ranged from 62.5 to 375 g/mL, while Ertugliflozin concentrations ranged from 0.9375 to 5.625 g/mL. At each stage, the average percentage recovery was not less than 98 percent and not more than 102 percent. Changes in flow rate, mobile phase composition, and temperature were used to assess robustness. [26]

Syed Wajahat Shafaat, et al. established and validated an analytical method for simultaneous quantification of ertugliflozin and metformin HCl in bulk and pharmaceutical dosage form using an HPLC gradient type experiment with a C18 (250 4.6 mm) column. The mobile phase consisted of a 65:35 v/v mixture of potassium dihydrogen phosphate buffer and methanol, with a flow rate of 1.0 mL/min. The detection was carried out in a UV detector with a wave length of 220 nm and a run time of 6 minutes. Ertugliflozin and metformin HCl elution peaks at 3.2 and 2.1 minutes, respectively. [27]

A simple, specific, quick, sensitive, precise, accurate, and stability indicating RP-HPLC technique for the simultaneous measurement of ertugliflozin pidolate and metformin hydrochloride in bulk and tablets was developed and validated by **K. Sravana Kumari and Sailaja Bandhakavi, et al.** The separation of ertugliflozin pidolate and metformin HCl was achieved isocratically on a Kromasil C18 column (150 mm 4.6 mm, 5 m) with a mobile phase of 0.1 percent ortho-phosphoric acid buffer (pH 2.7): acetonitrile (65:35 percent v/v) pumped at a flow rate of 1 ml/min and a column temperature of 30 ° As a diluent, HPLC grade water: ACN (1:1) was utilised. A total of 10 l of the medicines' standard solution was administered. At 224 nm, the eluted analytes were identified. With a run time of 5.0 minutes, metformin HCl was eluted at 2.170 minutes and ertugliflozin pidolate at 2.929 minutes. With a correlation coefficient of 0.999 for both medications, the devised approach was found to be linear in the concentration ranges of 0.9375–5.625 g/ml for ertugliflozin pidolate and 62.5–375 g/ml for metformin HCl. The LOD for ertugliflozin pidolate and metformin HCl, respectively, were 0.025 g/ml and 0.87 g/ml. Ertugliflozin pidolate and metformin HCl had LOQs of 0.076 g/ml and 2.63 g/ml, respectively. Conclusion: Simple, quick, sensitive, accurate, precise, linear, and stability-

indicating, the developed RP-HPLC technique for simultaneous quantification of ertugliflozin pidolate and metformin HCl in bulk and tablets was developed. As a result, the devised method might be used to monitor the quality of medications in bulk and tablets on a regular basis. [28]

For the investigation of simultaneous evaluation of Ertugliflozin and Metformin in tablet dosage forms,

Bhawani Sunkara et al. established a simple, inexpensive, sensitive, authentic, and faithful technique. The chromatographic analysis was carried out isocratically using a Phenomenex C18 column (150 mm 4.6 mm, 5 m) and a mobile phase containing acetonitrile and 0.1 percent OPA buffer in a 40:60 percent v/v proportion was passed throughout the column at a flow rate of 1 ml/min at 30 °C. The analytes were eluted at 220.0 nm after about 10 l of drug solution was injected. Ertugliflozin and Metformin elution times were 2.226 minutes and 2.955 minutes, respectively. Ertugliflozin and Metformin have percentage RSDs of 0.60 and 0.59, respectively. Ertugliflozin and Metformin's percentage recoveries were determined to be 100.55 percent and 99.40 percent, respectively. Metformin and Ertugliflozin were shown to have LOD and LOQ values of 0.10, 0.2, and 0.03, 0.09 g/ml, respectively. Ertugliflozin's regression equation was y = 11287x + 1191, while Metformin's was y = 46270x + 161.0. According to the ICH recommendations, all verification parameters are within the range, and the degradation products are also within the limits, indicating that the procedure is stable. Conclusion: The elution time and run time in the currently proposed RP-HPLC analytical method have been lowered, demonstrating that the method is cost-effective and widely accepted, as well as easy and practical, and may be utilised in routine quality control tests in the industry. [29]

CONCLUSIONS

For estimating Ertugliflozin in bulk and pharmaceutical dose forms, the majority of the methods discussed utilised HPLC with UV detection. For the estimation of medication in biological fluids, bioanalytical procedures such as HPLC and LC MS/MS were utilised. Multiple spectroscopic approaches such as Fluorescence spectroscopy, Fluorescence life time, and 3D fluorescence spectroscopy were used to study the interaction of ertugliflozin with human serum albumin in vitro. The pharmacokinetics of Ertugliflozin and its fixed dosage combinations were studied using HPLC and LC MS/MS. Various spectrophotometry and chromatographic procedures were described in a systematic and easy-to-understand manner.

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