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A COMPREHENSIV REVIEW ON ANALYTICAL METHODS FOR ESTIMATION OF DEXTROMETHORPHAN AND SITAGLIPTIN

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ABSTARCT:
Dextromethorphan Hydrobromide is a non-selective serotonin uptake inhibitor and an agonist of sigma-1 receptor, and acts centrally to elevate threshold for coughing. Sitagliptin, the dipeptidyl peptidase-4 (DPP-4) inhibitor, is used to treat type 2 diabetes. Their physicochemical characteristics, modes of action, and clinical significance are all thoroughly covered in this review. For the evaluation of both medications separately and in combination with other agents, it also provides a summary of official pharmacopeial procedures and reported analytical techniques, such as HPLC, RP-HPLC, HPTLC, Spectrophotometry, and Micellar Liquid Chromatography. The progress and difficulties in method development and validation are highlighted by a critical assessment of chromatographic parameters, detection wavelengths, and mobile phases. This review provides a comprehensive reference for researchers and analysts working on dextromethorphan and sitagliptin, highlighting the importance of reliable, sensitive, and stability-indicating techniques for routine quality control and pharmacokinetic investigations.

KEYWORDS: DeXtroMethorphan HydroBromide; Sitagliptin Phosphate; Analytical method development; HPLC; UV HPLC; RP-HPLC; HPTLC; Drug profile; Pharmacopeial Methods.

1. INTRODUCTION

Drug research, quality assurance, and therapeutic monitoring all depend heavily on the precise and trustworthy assessment of pharmaceutical components. Because of their unique pharmacological activities, Dextromethorphan and Sitagliptin stand out among the wide variety of active pharmaceutical ingredients (APIs) in terms of therapeutic significance.

Dextromethorphan Hydrobromide (DXHB) has been used as an Antitussive for more than 50 years. It can be used individually or in combination.[1] DXHB is a non-selective serotonin uptake inhibitor and an agonist of sigma-1 receptor, and acts centrally to elevate threshold for coughing.[2] DXHB's action on the N-methyl-D-aspartate receptor may contribute to its antitussive properties, including for coughing in Palliative care.[3]

Millions of new cases of type 2 diabetes mellitus are reported worldwide each year, making it a prevalent and quickly expanding disease. Diabetes has grown to be a major health concern for people and has a huge financial impact on families, individuals, and the global health system.[4] One of the

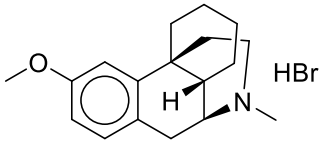
main causes of death worldwide, diabetes and its complications are thought to have claimed the lives of about 5 million people in 2015. [5,6]
On the other hand, the Dipeptidyl Peptidase-4 (DPP-4) inhibitor Sitagliptin, is used to treat type 2 diabetes. Sitagliptin improves glycaemic management by raising the levels of incretin hormones through the inhibition of the DPP-4 enzyme. Sitagliptin is subject to strict analytical standards for dosage accuracy, stability testing, and bioequivalence studies, and it is frequently taken in combination therapy. A new class of anti-hyperglycaemic drugs called Dipeptidyl Peptidase-4 (DPP-4) inhibitors works by breaking down and deactivating glucagon-like peptide-1 (GLP-1). These drugs are used to treat Type 2 diabetes mellitus. An incretin hormone called GLP-1 promotes the production and secretion of insulin, suppresses the release of glucagon in a glucose-dependent way, facilitates stomach emptying, and decreases appetite. [7,8,9,10,11]

Although both medications are well-known in their respective fields of medicine, growing interest in creating combination treatments or researching drug-drug interactions calls for the development of analytical methods that can estimate both compounds separately or at the same time. These techniques need to handle issues with varying chemical structures, solubility profiles, and sensitivity of detection. The goal of this review is to give a thorough summary of the many analytical techniques used to estimate Sitagliptin and Dextromethorphan. It talks about the advantages and disadvantages of both sophisticated approaches like liquid chromatography-tandem mass spectrometry (LC-MS/MS) and more traditional ones like UV spectrophotometry, High-performance liquid chromatography (HPLC), and Ultra-performance liquid chromatography (UPLC). Particular attention is paid to the analytical characteristics that affect method development and validation, as well as the possibility of simultaneous estimation.

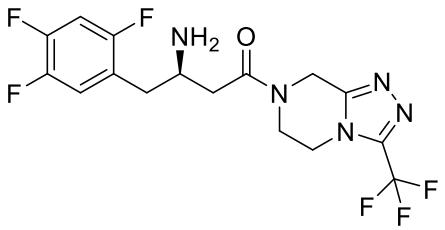
These analytical processes are developed and validated in accordance with ICH Q2(R1) requirements to guarantee that they achieve essential parameters such as linearity, precision, accuracy, limit of detection (LOD), limit of quantitation (LOQ), and robustness. A thorough examination of these analytical procedures is required for researchers, analytical scientists, and regulatory agencies to assess current advancements, compare methodology, and suggest future directions in the estimate of these therapeutically significant substances.

2. DRUG PROFILE

2.1 DEXTROMETHORPHAN HYDROBROMIDE (DXHB). [12]

IUPAC NAME	(1S,9S,10S)-4-methoxy-17-methyl-17-azatetracyclo [7.5.3.$0^{1,10}$.$0^{2,7}$]heptadeca-2(7),3,5-triene
MOLECULER FORMULA	$C_{18}H_{26}BrNO$
CHEMICAL STRACTURE	
MOLECULAR MASS	352.32 g/mol
DISCRIPTION	White to off-white crystalline powder
SOLUBILITY	freely soluble in chloroform, soluble in ethanol, and sparingly soluble or slightly soluble in water
pH and pKa Value	pH of a 1% aqueous solution is around 5.2-6.8, 9.3-9.85
MELTING POINT	122-126 ℃
CAS No.	6700-34-1
MECHANISM OF ACTION	Dextromethorphan is a low-affinity uncompetitive NMDA antagonist and sigma-1 receptor agonist. It is also an antagonist of α3/β4 nicotinic receptors. However, the mechanism by which dextromethorphan's receptor agonism and antagonism translate to a clinical effect is not well understood.

2.2 SITAGLIPTIN PHOSPHATE [13]

IUPAC NAME	(3R)-3-amino-1-[3-(trifluoromethyl)-6,8-dihydro-5H-triazolo[4,3-a] pyrazin-7-yl]-4-(2,4,5-trifluorophenyl) butan-1-one; phosphoric
MOLECULER FORMULA	$C_{16}H_{20}F_6N_5O_6P$
CHEMICAL STRACTURE	
MOLECULAR MASS	523.32 g/mol
DISCRIPTION	Typically formulated as a crystalline solid, often a monohydrate form
SOLUBILITY	Sitagliptin phosphate is highly soluble in water at mildly acidic pH (~69 mg/mL at pH 4.5), moderately soluble in neutral buffers (~5 mg/mL in PBS pH 7.2)
pH and pKa Value	Sitagliptin is a weak base with a basic pKa in the range of 7.7 to 8.8, and in aqueous form (particularly as a salt), its solution pH commonly falls between 4.5 and 6.0.
MELTING POINT	194.0 to 198.0 ℃
CAS No.	654671-77-9.
MECHANISM OF ACTION	Inhibition of DPP-4 by sitagliptin slows DPP-4 mediated inactivation of incretins like GLP-1 and GIP. Incretins are released throughout the day and upregulated in response to meals as part of glucose homeostasis. Reduced inhibition of incretins increases insulin synthesis and decrease glucagon release in a manner dependant on glucose concentrations. These effects lead to an overall increase in blood glucose control which is demonstrated by reduced glycosylated haemoglobin (HbA1).

2.3 Implications for Analytical Method Development [14]

The distinct chemical nature and Pharmacological classification of Dextromethorphan and Sitagliptin pose unique challenges in analytical method development.

Differences in:

- Polarity and solubility,
- UV absorbance spectra,
- Stability under stress conditions, and
- Detection sensitivity requirements

3. Literature Survey and Research Gap

For pharmaceutical compounds, the creation of accurate and verified analytical techniques is essential to guaranteeing medication safety, effectiveness, and regulatory compliance. Many analytical methods have been investigated for the individual estimation of Dextromethorphan and Sitagliptin over the last few decades, with notable developments in the spectroscopic and chromatographic domains. There is a significant vacuum in the literature, nevertheless, as only a small number of research have tried their simultaneous estimation.

3.1 Review of Analytical Methods for Dextromethorphan

Dextromethorphan has been extensively analysed in various dosage forms using:

- UV–Visible spectrophotometry, due to its strong absorbance in the UV range (225–280 nm).[15]

- HPLC and RP-HPLC methods, utilizing C18 columns with mobile phases comprising acetonitrile or methanol in phosphate buffer.[16]
- Gas chromatography (GC), particularly in forensic and toxicological studies for detecting dextromethorphan in biological matrices.
- LC-MS/MS, providing high sensitivity and selectivity in plasma or serum for pharmacokinetic and abuse studies.[17]

These methods have been validated in line with ICH guidelines and are widely accepted in both quality control and research environments.

3.2 Review of Analytical Methods for Sitagliptin

For Sitagliptin, numerous methods have also been reported, including:

- UV and derivative spectrophotometry, often in combination with metformin or other antidiabetics.[18]
- RP-HPLC, used for estimation in bulk and dosage forms, especially stability-indicating methods.[19]
- UPLC, offering faster separation and enhanced resolution for high-throughput settings.[18]
- LC-MS/MS, extensively applied in bioanalytical contexts due to Sitagliptin's low plasma concentration and need for high sensitivity.[20]

Some researchers have also explored green analytical chemistry approaches and QbD (Quality by Design) techniques to optimize conditions for Sitagliptin analysis.

4. VARIOUS ANALYTICAL TECHNIQUES FOR THE ESTIMATION OF DEXTROMETHORPHAN HYDROBROMIDE

Due to its significant use in cough suppressants and over-the-counter (OTC) formulations, Dextromethorphan has been the focus of a great deal of analytical research. Numerous methods for both qualitative and quantitative estimation in biological and pharmaceutical matrices have been developed and validated. The most popular and successful techniques for estimating Dextromethorphan are highlighted in this section, along with their unique advantages, disadvantages, and strengths.[14]

4.1 UV–Visible Spectrophotometry:

UV spectrophotometry is one of the simplest and most cost-effective techniques for estimating Dextromethorphan, particularly in bulk drugs and single-component formulations.

A 10 ml volumetric flask was filled with 1 ml of the standard stock solution (100µg/ml), which was diluted with 0.1N HCl to a concentration of 10µg/ml. Using 0.1N HCl as a blank, the absorbance of the resultant solution was measured in a 1 cm cell in the UV spectrometer's 200–400 nm range, and the spectra was recorded. The greatest absorbance in the DXM spectra was seen at 278 nm. DXM's linearity was determined to be between 10 and 30 µg/ml, with a correlation coefficient of 0.9993. DXM was found to have a LOQ of 1.30µg/ml and a LOD of 3.93µg/ml. Linear regression equations were used to determine the medication concentrations. 99.99% of the total was found. [21]

Advantages:

- Rapid and inexpensive
- Minimal sample preparation
- Suitable for preliminary assays

Limitations:

- Lack of specificity in the presence of other absorbing substances
- Not suitable for biological fluids

4.2 High-Performance Liquid Chromatography (HPLC):

HPLC is the most widely used technique for accurate quantification of Dextromethorphan in formulations.

Using ethanol as a solvent, the double divisor ratio spectra derivative spectrophotometry method was created to measure the amounts of dextromethorphan hydrobromide in tablet dosage form. The technique is based on measuring at either the maximum or minimum wavelengths and using the coincident spectra of the derivative of the ratio spectra that are obtained using a double divisor (sum of two spectra). After that, the technique was used to find out how much Dextromethorphan Hydrobromide was present in the tablet dosage form. The first derivative at Δλ 2 (λ 286.1 nm) was subjected to the double divisor ratio spectra derivative spectrophotometry method in order to determine the amount of dextromethorphan hydrobromide. The best results are obtained when wavelengths are chosen based on wavelengths. The average percentage of recoveries was 99.95%. According to the recovery study, the technique is effectively used to evaluate Dextromethorphan Hydrobromide in pharmaceutical formulation without interference from excipients. Every validation parameter fell within the permissible bounds.[22]

A straightforward, quick, and accurate spectrophotometric technique has been created to assess the improvement in Dextromethorphan's water solubility. The absorbance served as the basis for the method. Using hydro trope dextromethorphan in double-distilled water as the solvent, the highest dextromethorphan was detected at 278 nm. With a correlation coefficient of 0.9993, linearity was achieved within the concentration range of 10–120 µg/ml. The intra-day and inter-day percentage RSDs were determined to be 0.8182 and 0.9438, respectively. The LOD and LOQ values were determined to be 3.76 and 1.141, respectively.[23]

Advantages:

- High sensitivity and specificity
- Suitable for multicomponent formulations
- Validated methods available for various dosage forms

Limitations:

- Requires expensive instrumentation and solvents
- Longer run times in some cases

4.3 Reversed-Phase High-Performance Liquid Chromatography (RP-HPLC):

Guaifenesin and dextromethorphan impurities in pharmaceutical formulations can be simultaneously estimated using a sensitive, stability-indicating gradient RP-HPLC technique. On a Sunfire C18, 250 × 4.6 mm, 5 µm column, effective chromatographic separation was accomplished using a mobile phase that contained a gradient mixture of solvents A and B. The mobile phase flow rate was 0.8 mL min−1, the detection wavelength was set at 224 nm, and the column temperature was 50°C. According to regression analysis, the correlation coefficient (R value) for guaifenesin, dextromethorphan, and their impurities was higher than 0.999. The formulation sample of guaifenesin and dextromethorphan was exposed to oxidative, acidic, basic, hydrolytic, thermal, and photolytic degradation stress conditions. Under conditions of peroxide stress, dextromethorphan was shown to significantly degrade while guaifenesin was found to remain stable. The breakdown products from dextromethorphan, guaifenesin, and their contaminants were clearly separated. The results of the peak purity test demonstrated the method's stability-indicating capabilities by confirming that the Guaifenesin and Dextromethorphan peak was uniform and pure in all stress samples and that the mass balance was greater than 98%.[24]

For the simultaneous measurement of Doxylamine Succinate and Dextromethorphan HBr in pharmaceutical dosage forms, an additional RP-HPLC method was created. ACN: Water (70: 30 v/v) pH was adjusted to 3.4 using Glacial Acetic Acid as the mobile phase, with a flow rate of 1 mL/min. The estimate was carried out using a Purospher® STAR RP18 end-capped (250 x 4.6) mm, 5µ) column as the stationary phase. At 250 nm, the effluents were observed. Dextromethorphan HBr and Doxylamine Succinate were shown to have retention times of 7.72 and 5.83 minutes, respectively. For Doxylamine Succinate and Dextromethorphan HBr, the method exhibits linearity in the concentration range of 20.84-62.51µg/mL and 50.02-150.07µg/mL, respectively. There was no evidence of any excipient interference with this approach. Recovery investigations for Dextromethorphan HBr and Doxylamine Succinate in formulations showed that they ranged between

98 and 99% and 98.0 and 103.0%, respectively. The specificity, precision, linearity, accuracy, LOD, LOQ, and robustness of this created method were all validated. Dextromethorphan HBr and Doxylamine Succinate recovered in formulations were found to be between 99.50-101.30% and 99-73-100.7%, respectively.[25]

Advantages:

- Robust and reproducible
- Suitable for single and combination drugs
- Can detect degradation products under forced conditions

Limitations:

- Moderate sensitivity
- Requires method optimization for complex matrices

4.4 Liquid Chromatography–Tandem Mass Spectrometry (LC–MS/MS):

Liquid chromatography coupled with tandem mass spectrometry is increasingly used for bioanalytical estimation of Dextromethorphan and its active metabolite, Dextromethorphan.

In a high throughput toxicology lab context, the LC-MS-MS technology has been developed to quantify Dextromethorphan and Dextrorphan in oral fluid. Following the recommendations of the Scientific Working Group for Forensic Toxicology, the devised approach was validated. Dextromethorphan and dextrorphan had a linear dynamic range of 5–100 ng/mL and a lowest limit of quantification (LLOQ) of 5.0 ng/mL. Overall, the precision and accuracy values for both medications fell within the acceptable range. Additionally, the LC-MSMS method's selectivity, matrix effect, and recovery were computed. To assess the method's applicability, 59 authentic samples were evaluated. Two samples tested positive for Dextromethorphan alone, whereas thirty samples tested positive for both Dextromethorphan and dextrorphan.[26] To determine the levels of dextromethorphan and dextrorphan in human oral fluid, a straightforward technique utilizing LC-MS/MS was created and verified. A phenyl column with isocratic elution (1 ml/min) of 10 mM ammonium-formate buffer and acetonitrile (65:35; v/v) with 0.1% formic acid was utilized for chromatographic separation after protein precipitation. Dextrorphan and dextromethorphan had retention durations of 2.6 and 5 minutes, respectively. It ran for seven minutes in total. For dextrorphan (1–100 ng/ml) and dextromethorphan (5–1000 ng/ml), the intra- and inter-assay variances (accuracy) varied from -13.6 to 8.8% and -9.6 to 5.7%, respectively. Variations in precision were ≤7.5%. It had a matrix effect of ≤11.8%.[27]

Advantages:

- Sub-ng/mL sensitivity
- Simultaneous quantification of parent drug and metabolites
- Minimal interference from biological matrices

Limitations:

- Expensive instrumentation and skilled personnel required
- Complex validation process

4.5 High-Performance Thin Liquid Chromatography (HPTLC):

A simple, sensitive and accurate stability indicating HPTLC method has been developed and validated for estimation of Dextromethorphan hydrobromide in bulk and pharmaceutical dosage form. On precoated silica gel 60 F254 aluminium plates, the drug was detected using a mobile phase consisting of Toluene: Methanol: Triethylamine (8.5:1:0.5 v/v/v). It was determined that the retention factor (Rf) was 0.60±1.92. The band was detected at 225 nanometers. A variety of stress conditions, including acid, base, neutral hydrolysis, oxidation, heat degradation, and photolysis, were applied to the medication. In compliance with ICH criteria Q2, the method was successfully validated (R1). With a correlation coefficient of 0.991, the results of the linear regression analysis showed a solid linear association spanning the 2000–20,000 ng/band concentration range. Since the recovery trials' results are nearly 100%, the approach was determined to be accurate.[28]

5. Analytical Techniques for Sitagliptin Estimation [18]

Due to its low dosage, frequent use in Fixed-Dose combinations, and probable degradation under a variety of stress conditions, sitagliptin, a selective DPP-4 inhibitor used in the treatment of type 2 diabetes mellitus, requires sensitive and accurate analytical techniques. Numerous methods for estimating it in biological matrices, pharmaceutical formulations, and bulk have been devised. This section examines several analytical techniques, emphasizing their methodology, benefits, drawbacks, and applicability to different situations**.**

5.1 UV–Visible Spectrophotometry

Sitagliptin exhibits characteristic UV absorbance, making it suitable for simple spectrophotometric estimation, particularly in formulations.

Metformin and sitagliptin combined in tablet form are estimated using the UV Spectrophotometric method. While metformin shows maximum absorbance at 237 nm, sitagliptin shows highest absorbance at 267 nm when diluted with distilled water. The calibration curves for metformin and sitagliptin were linear between 4 and 14 µg/ml and 10 and 300 µg/ml, respectively. The maximum percentage RSD was less than 2 percent. The recommended approach was shown to have a recovery percentage of 97.12 to 99.46% for sitagliptin and 98.15 to 99.85% for metformin. The LOD of the recommended method was 0.8952 µg/ml for metformin and 0.397 µg/ml for sitagliptin. The LOQ for metformin was 2.7159 µg/ml, whereas that of sitagliptin was 1.2951 µg/ml. [29]

Sitagliptin Phosphate can be quantitatively determined in bulk and pharmaceutical formulations using a straightforward, sensitive, repeatable, and economical stability-indicating UV spectrophotometric technique. After scanning the UV spectra between 200 and 400 nm, the highest wavelength for absorption was determined to be 267 nm. In the concentration range of 10–100 µg/ml, Beer's law was followed. The technique was successfully used to the pharmaceutical dosage form containing the aforementioned drug without any interference from the excipients, yielding good accuracy (99.87-100.45%) and precision (%RSD 1.3147-1.2957). It was determined that the limits of quantification and detection were 0.45 µg/ml and 0.16 µg/ml, respectively.[30]

Advantages:

- Economical and quick
- Useful for routine formulation analysis
- No need for complex instrumentation

Limitations:

- Lower sensitivity
- Less selective in presence of co-formulated drugs or excipients

5.2 High-Performance Liquid Chromatography (HPLC):

A HPLC method for the estimation of Sitagliptin phosphate monohydrate in bulk and its pharmaceutical dosage form. The mobile phase used for the chromatographic separation was 0.01M KH2PO4: Methanol in a 50:50% v/v ratio, with pH 2.5 adjusted by 0.2% orthophosphoric acid. Using PDA detection at 267 nm, the Zorbax Eclipse XDB C18 column (150×4.6 mm, 5µ) had a flow rate of 0.7 ml/min. The correlation coefficient was 0.999 and the described approach was shown to be linear for the 5- to 30-µg/ml range. The Sitagliptin assay yielded a 99.89% result. The study's findings demonstrated the simplicity, speed, accuracy, precision, dependability, and economy of the suggested RP-HPLC method, making it a valuable tool for routinely determining sitagliptin phosphate in bulk and in pharmaceutical dose form.[31]

Advantages:

- Enhanced specificity over basic UV methods
- Useful for resolving overlapping spectra

Limitations:

- Limited to formulations with low matrix complexity
- Less sensitive than chromatographic methods

5.3 High-Performance Thin Liquid Chromatography (HPTLC):

A new simple high performance thin layer chromatographic method for simultaneous determination of antidiabetic drugs, metformin hydrochloride and sitagliptin phosphate in bulk and tablet dosage form. Chromatographic separation of the drugs was performed on aluminum plates precoated with silica gel 60 F254 as the stationary phase and the solvent system consisted of acetone: methanol: toluene: formic acid (4:3:2:1 v/v/v/v). The method was validated by doing a densitometric examination of the separated zones at 220 nm. Metformin hydrochloride and sitagliptin phosphate had Rf values of 0.36 ± 0.02, 0.63 ± 0.02 and 100.1% and 99.84%, respectively. For metformin hydrochloride and sitagliptin phosphate, the calibration curves of peak area versus concentration were linear from 2000–5000 ng per band and 200–500 ng per band, respectively, and the regression coefficient (r2) was higher than 0.99. Metformin hydrochloride and sitagliptin phosphate had respective LODs of 45 and 27 ng per band and LOQs of 150 and 87 ng per band. In accordance with ICH criteria, the method's linearity, precision, robustness, and assay applicability were validated.[32]

Advantages:

- Robust and reproducible
- Suitable for single and combination drugs
- Can detect degradation products under forced conditions

Limitations:

- Moderate sensitivity
- Requires method optimization for complex matrices

5.4 Ultra-Performance Liquid Chromatography (UPLC):

UPLC offers faster, high-resolution separation of Sitagliptin with improved peak sharpness and shorter run times compared to conventional HPLC.

UPLC method for the estimation of Sitagliptin in pharmaceutical dosage form. Phosphate buffer (pH 6) and acetonitrile (70:30, v/v) were used as the mobile phase in an X-bridge C18 column (4.6 i.d. × 150 mm, 5 µm particle size) at a flow rate of 1 ml/min at 268 nm utilizing a photodiode array plus (PDA+) detector. At 4.607 minutes, the retention time was discovered. With a LOD value of 0.06 µg/ml and a LOQ of 0.225 µg/ml, the linear regression analysis results for the linearity plot displayed correlation coefficient values of 0.999. For both intra-day and inter-day precision, the relative standard deviation (% RSD) was less than 2.0%. With recovery percentages ranging from 98.50 ± 0.03 to 99.70 ± 0.05 and an RSD of less than 2, the approach was determined to be accurate.[33]

Advantages:

- High sensitivity and resolution
- Fast, cost-effective in large-scale labs

Limitations:

- Requires specialized instrumentation
- Initial setup cost is high

5.5 Liquid Chromatography–Tandem Mass Spectrometry (LC–MS/MS):

LC-MS/MS is widely used for bioanalytical estimation of Sitagliptin in plasma, serum, and other biological fluids.

Ertugliflozin and Sitagliptin is combination of Antidiabetic drug, a member Antidiabetic drug, is a recent drug developed by Merck Sharp and Dohme Company for the treatment of Type 2 diabetes. Ertugliflozin and Sitagliptin can be used alone or in combination therapy. We used a Phenomenex Gemini, C18 (150 × 4.6 mm, 5 µm) column for chromatographic separation. The 0.1% formic acid:acetonitrile (10:90) v/v mobile phase, column temperature of 40°C, and flow rate of 0.6 mL/minutes formed the foundation of the isocratic technique. Using electrospray ionization, the mass spectrometer was run in multiple reactions monitoring (MRM) mode. Ertugliflozin's transition pair (precursor to product ion) was monitored at m/z 437.10-328.95 in the positive mode, and Sitagliptin's transition pair (precursor to product ion) was monitored at m/z 408.10-234.95 in the positive mode.

Ertugliflozin and sitagliptin were found to be linear in the concentration ranges of 15 to 450 ng/mL and 100–3000 ng/mL, respectively.[34]

Advantages:

- High specificity and sensitivity
- Suitable for pharmacokinetic and bioequivalence studies

Limitations:

- High equipment and operating costs
- Requires skilled personnel

5.6 CAPILLARY ELECTROPHORESIS:

A method for the simultaneous determination of sitagliptin (SG) and metformin (MF) in pharmaceutical preparations. Separation was carried out in fused silica capillary (50.0 cm total length and 43.0 cm effective length, 49 µm i.d.) by applying a potential of 15 KV (positive polarity) and a running buffer containing 60 mM phosphate buffer at pH 4.0 with UV detection at 203 nm. The capillary cartridge's temperature was maintained at 25 °C while the samples were hydrodynamically injected for three seconds at 0.5 pressure. The internal standard (IS) was phenformin. The technique's specificity, linearity, quantitation and detection limits, accuracy, precision, and robustness were all appropriately validated. With limits of detection of 0.49 and 2.11 µg/mL and limits of quantification of 1.48 and 6.39 µg/mL for SG and MF, respectively, the technique demonstrated high linearity in the ranges of 10–100 µg/mL and 50–500 µg/mL. Their percentage relative standard deviation values (% R.S.D.) were 1.50% (n = 3), and the estimated amounts of SG/MF were nearly equal with the verified values.[35]

6. Summary

Both Dextromethorphan and Sitagliptin have well-established analytical methods individually; however, method development for simultaneous estimation requires a balanced approach incorporating sensitivity, selectivity, speed, and cost-effectiveness. Chromatographic methods, particularly RP-HPLC and LC-MS/MS, stand out as the most versatile platforms capable of addressing diverse analytical needs.

7. Discussion and conclusion

The quality, safety, and effectiveness of pharmaceutical formulations as well as clinical monitoring depend on the estimation of Dextromethorphan and Sitagliptin using a variety of analytical techniques. From basic UV spectrophotometry to sophisticated hyphenated techniques like LC-MS/MS, this review covers a wide range of analytical techniques, each with its own merits and disadvantages.

Rigorous method validation aligned with international regulatory guidelines ensures the reliability and reproducibility of these analytical procedures, facilitating their application in quality control, pharmacokinetic studies, and therapeutic drug monitoring.

Looking forward, the integration of green chemistry principles, automation, and artificial intelligence in analytical method development promises to enhance efficiency, reduce environmental impact, and support personalized medicine initiatives.

In summary, continued advancements and optimization in analytical methodologies for Dextromethorphan and Sitagliptin will play a pivotal role in supporting pharmaceutical innovation and improving patient outcomes.

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