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# Overview on remogliflozin SGLT-2 inhibitor in the management of type-2 diabetic mellitus in human beings

Sodium-glucose transport protein 2 inhibitors have become a significant category of oral medications in order to manage type 2 diabetic mellitus, particularly in people with heart disease or kidney disease, and have been highly advised overall current studies advice on how to treat. They can reduce blood pressure and help people lose weight, but they also come with drawbacks like genitourinary infections. The newly approved remogliflozin combinations are the product study of the pharmaceutical business for a new pharmaceutical class and novel drug combination with a view to managing diabetes. Remogliflozin etabonate is the term for the remogliflozin ester form. This study examines the clinical effectiveness, safety profile, pharmacokinetics, and pharmacodynamics of remogliflozin etabonate. However, its analytical profiling using RP-HPLC, UV, RP-UPLC, HPTLC, and LC/MS. this review addresses the individual experiments conducted during the development of analytical method for remogliflozin etabonate.

*Keywords*: Remogliflozin Etabonate, SGLT-2 Inhibitor, Type-2 Diabetic Mellitus, Analytical Method.

## *Introduction*

Type 2 diabetes is a complicated metabolic condition that frequently needs several Therapy approaches to be effectively treated. The 2 sodium-dependent glucose transporteris inhibited (SGLT-2) gives a unique therapeutic strategy for type 2 diabetes using enhanced renal glucose excretion, it brings down blood sugar and results in losing weight [1]. Numerous specific sglt2 inhibitors are being developed or are already in use [2]. Selective SGLT2 inhibitors are being created or are already in use in numerous applications. [3].

The goal of this trial was to assess the effectiveness, security, and tolerability of daily one remogliflozin (RE) given to type 2 diabetic patients for a period of 12 weeks as a monotherapy, oral drug class of the new generation (t2dm). They work by increasing blood sugar levels are lowered by urinating glucose out. They benefit patient in the presence of insulin resistance or decreased pancreatic function due to their distinct insulin-independent mode of action.

They inhibitors of SGLT-2 are a common type 2 diabetes mellitus are known to enhance renal function, lower the especially beneficial in patients are SGLT-2 with hypertension and high risk of hypoglycaemia [4-6].

Worldwide, kind 2 diabetic mellitus incidence and prevalence are growing, along with 90% of adults having diabetes mellitus and one in eleven having t2dm. China and India are the diabetes epidemic's epicentres in Asia [7]. Today, 8.9% of India's population, or 77 million people, have diabetes [8]. Guidelines for t2dm management are offered in accordance with the American organization of clinical endocrinologists. They incorporate lifestyle counselling, weight loss with medical assistance, and personalized targets for reaching a haemoglobin a1c (hba1c) level of 6.5%.selection of antidiabetic agents is based on the traits of the patient, including lifestyle, co-morbidities, weight, glycemic index, and unfavourable side effects of pharmacotherapy. Digestive problems, hepato-renal damage, hyperinsulinemia-related weight gain, and hypoglycemia are the adverse consequences of oral medicines that treat diabetes that are frequently reported [9, 10]. A safer anti-diabetic drug is necessary given the rise in adverse effects, long-term negative effects, possibility for weight gain with this medication, and hypoglycemia are the critical effects to be consider [11].

*Review*

**History and Development of RemogliflozinRegimen**

Japan's Kissei pharmaceutical company made the initial discovery of remogliflozin; and was later created byBHV pharma, a joint venture between Glaxosmithkline and Glenmark [12]. Remogliflozin has been tested on 2500 people from different ethnic backgrounds in 26 registered trials worldwide [13]. A phase 3 study and two pharmacokinetic (PK) studies, and a clinical trial for this medication were all carried out Indian (CTRI/2017/06/0088887, 2017/07/009121, and 2017/10/010043) [14-16]. Glenmark pharmaceuticals gained regulatory authorization for 100 mg pills to administered twice daily for t2dm in April 2019 following the conclusion of In a phase-3 clinical investigation, remogliflozin etabonate showed its Comparing efficacy and safety to dapagliflozin [17, 18]. Glenmark then introduced remogliflozin on the market in India, and under a sub-licensing deal, an Indian company named torrent pharmaceuticals took over marketing [19, 20]. After Glenmark released remogliflozin onto the Indian market, torrent pharmaceuticals, an Indian business, took over marketing as part of a sub-licensing agreement [21]. Remogliflozin and remoglifozin-metformin combination are safe and effective for treating type 2 diabetes in a real-world context, according with regard to a potential active post-marketing surveillance research called the reform India trials, which was started in November 2019 [22, 23]. A Phase II study of remogliflozin for non-alcoholic steato-hepatitis etabonate in rash In the US, a patient (rein) research is now in progress in addition to these Indian investigations. A Phase-I study of the obesity drug remogliflozin and a Phase-I experiment for people with type 1 diabetes were both stopped in us in May 2019 for unknown reasons [24].

**Mechanism of Action** (Fig. 1, 2)**:**

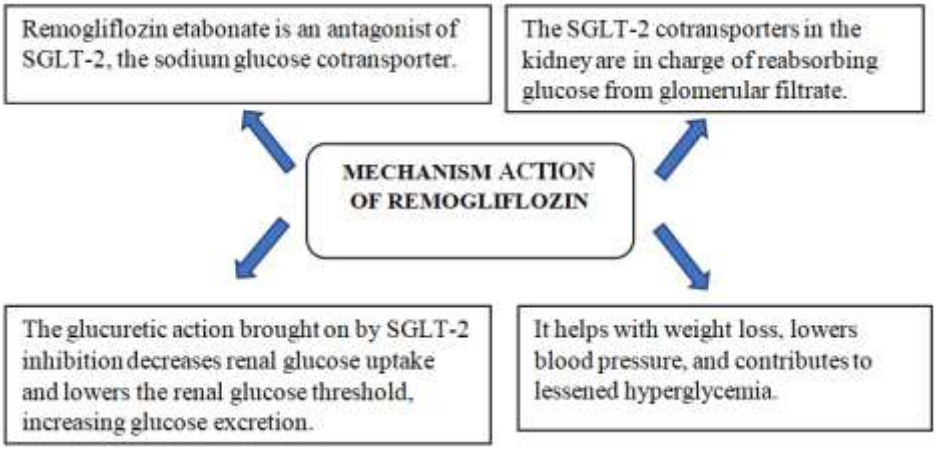


Figure 1. Mechanism of action of remogliflorzin

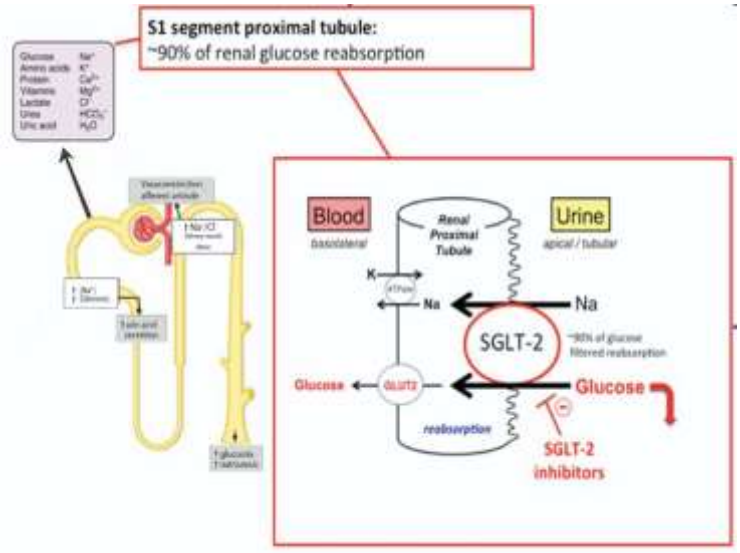


Figure 2. Mechanism of action of SGLT-2 inhibitor

**Pharmacological Profile**

**Pharmacodynamics**

Remogliflozin having *in vitro* ki values for human slgt1 and 2 of 4520 and 12.4 nm, respectively [25]. Remogliflozin etabonate, when given orally in standard rats and mice, an amount-dependent rise in urine insulin excretion and a fall in plasma insulin concentrations *in vivo*. In normal and streptozotocin-induced diabetic rats, delivering a single oral dosage decreased the rise as a result of glucose loading in plasma glucose in a dose-dependent manner, with the latter group showing a noticeably improved effect [25]. Remogliflozin etabonate was given orally in a single dosage to db/db mice. remogliflozin etabonate was also found to lower fasting blood sugar, glycated haemoglobin (hba1c), and insulinand urine expelling glucose in db\db mice when given orally once daily for six weeks. Remogliflozin etabonate, when taken orally for eight weeks, reduced hyperglycaemia, hyperinsulinemia, hypertriglyceridemia, and having a high-fat diet causes insulin resistance in goto-kakizaki rats [25]. The drug remogliflozin etabonate was given orally and decreased plasma lipids by 40%, hepatic lipid content by 42%, and liver weight by 42%. 76 and 48% decreases in the levels of alanine and aspartate aminotransferases, respectively when compared to a mouse model of non-alcoholic fatty liver disease [26]. Remogliflozin etabonate was given to healthy volunteers (50–1000 mg) and t2dm patients (50 and 500 mg) in a phase I trial. This led to a rise in total urine glucose excretion that is dose-dependent from 0–24 h. the proportion of Filtered glucose load was comparable amongst the groups. When urine glucose excretion was adjusted in accordance with Plasma glucose levels and creatinine clearance in circulation (to calculate the proportion of filtered glucose load) [27, 28].

**Pharmacokinetics**

Pharmacokinetics after oral treatment, Ester prodrug remogliflozin etabonate is quickly riveted before being thoroughly gastrointestinal mucosa, where it is de-esterified to create the crucial element, which manifests most noticeably in the plasma. The metabolism of remogliflozin primarily by cytochrome p450 (CYP) 3a4 to GSK 279782 (the energetic metabolite) and GSK 333081 before being glucuronidase to form inactive glucuronide conjugates. Remogliflozin etabonate is taken orally after oral administration is quickly absorbed, and the gastrointestinal mucosa significantly de-esters it to the active molecule remogliflozin, that seems most prominently in plasma over 93% of [14] remogliflozin etabonate was absorbed, according to a mass balance investigation with a single dosage on healthy participants. remogliflozin is metabolised primarily by cytochrome p450 (CYP) 3a4 to GSK 279782 and GSK 333081, which then undergo glucuronidation to create [30]. Remogliflozin C max and AUC at constant state and in Indian individuals with t2dm was 559 ng/ml and 1861 ng/h/ml, respectively [29] about 65% of remogliflozin remained tethered to plasma protein. Remogliflozin neither differently transported toward plasma cells nor have they been found to selectively associate with tissues that contain melanin [29]. Cyp3a4 and CYP2C19 both significantly contribute to the metabolism of drug ketoconazole, a powerful cyp3a4 antagonist, demonstrating a modest hazard of medication interactions with drugs that suppress CYP [29] individuals with mildly implies some degree of renal impairment showed similar pharmacokinetic profiles for remogliflozin etabonate, indicating that dosage modifications are not required in these patients [31] when metformin is co-administered with 500 mg twice per day of remogliflozin etabonate in individuals with t2dm (n=13) there is no change in the steady-state pharmacokinetic profile [32, 33].

**Clinical Efficacy and Safety**

During phase III study, remogliflozin 100 mg twice daily for 24 weeks was given to those with uncontrolled type 2 diabetes hyperglycaemia who were receiving metformin alone. These participating patients noticed an early and steady decline in hba1c, with a decline of 0.72% at 24 weeks. At 24 weeks, a decrease with postprandial plasma glucose values of 39.2 mg/dl and 17.86 mg/dl, respectively, while fasting, was seen. After 24 weeks, a 2.7 kg decrease in body weight was seen. Systolic pressure decreased by 2.6 mmhg, and diastolic pressure decreased by 2 mmhg [34, 35] having a low prevalence of urinary tract infections (3.1%), mycotic infections in the vagina (1.7%), and hypoglycemia (1.3%) the whole unfavourable reactions occurring mid-treatment occurred 8.5% of the time. 100 mg bid of remogliflozin treatment was therefore determined must be efficient, secure, and well-tolerated [35, 36].

**Adverse effect**

During phase III trial mentioned above (ctri2017-07-009121), among the most commonly reported side effects were urinary tract infections, pyrexia, headaches, bacteriuria, constipation, diarrhoea, reduced glo-

merular filtration rate, ketonuria, cough, dyslipidaemia, asthenia, and viral infections [37] in the phase iii trial, individuals taking dapagliflozin or remogliflozin as a supplement using metformin reported hypoglycaemia in roughly equal amounts (2% in each treatment arm). There were 1.8%, 1.2%, and 2.7% of recipients 100 and 250 mg, respectively, of the medication remogliflozin etabonate, and recipients from dapagliflozin who reported having vulvovaginitis, balanitis, and other similar genital diseases, all of mild to moderate severity, all of which responded to a first round of conventional treatment. Urinary tract infections had been seen in 3.1% and 6.6% respectively. By people who took 100 and 250 mg of remogliflozin etabonate dapagliflozin patients in 2.1% of cases. Remogliflozin or Those who take dapagliflozin did not experience hypovolemia [37].

**Advantages and Limitations of Remogliflozin Etabonate Based on Available Data**

Advantages effectiveness that is acceptable, with an average hba1c reduction of 0.5% to 1.0% mild weight loss lower the risk of hypoglycaemia low possibility of contact with medications that block the p450 enzyme system overall, it was positively received. Limitations to obtain optimal efficacy, twice-daily dose could be recommended. Genital mycotic infections, urinary tract infections, and lightheadedness are typical side events (3–12% versus 0% placebo), must be examined as a supplement therapy, in the elderly, and in people with chronic renal disease lack of long-term safety and effectiveness data not published in another trial [38]. Additionally, urinary tract infections (UTI) were reported by 3-11% more frequently with re use compared to 0% with placebo [39, 40]. The higher prevalence of hereditary mycotic infections and urinarytract infection is most likely connected to the rise in urine glucose excretion caused by sglt2 inhibitors, whilst dizziness is most likely connected to dehydration as a result of their diuretic impact [41, 42] increased genital mycotic infection prevalence was linked to higher re dosages, but other negative side effects were not clearly associated with this trend [39, 40]. It was interesting and comforting that none of the two biggest re trials had hypoglycaemia documented [39, 40]. In fact, SGLT-2 inhibitors generally have a low risk of causing hypoglycaemia, with the exception of when they are used with sulfonylureas or insulin [41-43].

**Pharmacoeconomic consideration** (Table 1, 2).

Table 1

**Comparison of the prices of sglt-2 inhibitors on the Indian market**

| Sr.no. | Drug | Manufacture | Company name | Dose (in mg) | Cost per tables |
|---|---|---|---|---|---|
| 1 | Remogliflozin | Glenmark pharmaceuticals | Remo<br>Remozen | 100<br>100 | 12.5($0.17)<br>12.5($0.17) |
| | | Mankind pharma ltd | SGLTR | 100 | 12.6 ($ 0.17) |
| | | Torrent pharmaceuticals ltd | Zucator 100 | 100 | 12.6 ($ 0.17) |
| 2 | Empagliflozin | Lupin pharmaceuticals | Gibtulio | 25<br>10 | 57 ($ 0.76)<br>47 ($ 0.63) |
| | | Boehringer Ingelheim | Jardiance | 25<br>10 | 57 ($ 0.76)<br>47 ($ 0.63) |
| 3 | Dapagliflozin | Sun pharmaceutical industries ltd | Oxra | 10<br>5 | 52 ($ 0.69)<br>50 ($ 0.67) |
| | | Astrazeneca plc | Forxigo | 10<br>5 | 52 ($ 0.69)<br>50 ($ 0.67) |
| | | Abbott | Gledepa | 10<br>5 | 52 ($ 0.69)<br>50 ($ 0.67) |
| 4 | Canagliflozin | Johnson & Johnson Ltd | Invokana | 100 | 54.5 ($ 0.73) |
| | | USV ltd | Sulisent | 100 | 55 ($ 0.74) |
| | | Janssen pharmaceuticals | Motivyst | 300 | 120 ($ 1.6) |
| 5 | Ertugliflozin | Merck Sharp &Dohme Corp | Steglatro | 5<br>15 | 300($3.75)<br>310($3.89) |

Table 2

**Comparative costs of SGLT-2 inhibitors with dpp4 available in combination form**

| Sr.no. | Drug | Manufacture | Brand name | Dose (in mg) | Price per tablet |
|---|---|---|---|---|---|
| 1 | Dapagliflozin+Metformin | Sun pharmaceutical industries ltd | OxrametXR<br>Udapa-M | 10\500 | 15 |
| | | USVLTD | 500XR | 500 | 12.5 |
| 2 | Empagliflozin+Metformin | Boehringer Ingelheim | Jardiance met<br>12.5mg/500mg | 500<br>1000 | 40<br>42 |
| | | Lupin ltd | Gibtulio met<br>12.5mg/500mg | 500<br>1000 | 40<br>42 |
| 3 | Empagliflozin+ Linagliptin | Cipla ltd | Tiptengio | 10/5<br>25/5 | 75<br>82 |
| | | Boehringer Ingelheim | Glyxambi | 10/5<br>25/5 | 75<br>82 |
| 4 | Dapagliptin +Saxagliptin | Astrazeneca | Qtern | 5/10 | 46 |
| 5 | Ertugliflozin +Sitagliptin | Merck Sharp & Dohme Corp. | Steglujan | 5/100<br>15/100 | 1500<br>1500 |
| 6 | Remogliflozin etabonate + Vildagliptin + Metformin | Glenmark pharmaceuticals ltd | Remo-zen mv<br>Remo mv | 500<br>1000 | 16.5<br>17.5 |

**Analytical Method**

Analytical processes are created to compare certain chemical properties to predetermined acceptability criteria for those qualities. As a result, choosing the most accurate assay techniques to assess a drug's composition is a part of developing analytical methods. In order to obtain clean extract with good quality, sample preparation is crucial in bioanalysis. Effectiveness of extraction additionally, the analyte influences the detector choice. Conscientiousness span choosing an appropriate internal standard (ISTD) is also crucial. Bioanalytical method has development problem. The function of internal standard is to make up for getting precise findings and avoiding matrix effects.

**HPLC and RP-HPLC Method**

One of the most vital methods for separating proteins and the technique of choice for separating peptides is reversed-phase HPLC (RP-HPLC). In addition to being used on a large industrial scale for preparative purifications, RP-HPLC has also been used on a nano, micro, and analytical size. RP-HPLC is a crucial instrument in proteomic research because it works well with mass spectrometry. Complex protein-peptide combinations can be separated at attomolar levels for subsequent analysis using contemporary apparatus and columns.

**Nandeesha I tigimatha et. al in** 2020

By the HPLC method, a 4.6 mm x 250 mm x 5 m c18 kromasil column was used as the stationary phase, even if the mobility phase was containing a 0.02 m ammonium acetate buffer, acetonitrile, and tetrahydrofuran in that order (v/v), with the PH being corrected to 4.0 by 1.0 Orthophosphoric Acid (m-OPA). With a 2.0 millilitres per minute flow rate, 101 sizes of the sample injection, and a 228 nm detection wavelength, this experiment was completed. In the spectral UV approach pure ethanol was used to dilute the RMZ. At 228 nm, the remogliflozin had the highest absorption. Consequently, 228 nm was employed throughout the investigation to determine during the analysis for the purpose of determining RMZ, 228 nm was employed. The RTS for atorvastatin (ATST), an internal benchmark, and RMZ they were 6.2 and 7.0 minutes, respectively. It was discovered that the resolution between the peaks was greater than 2.0. There were 10 minutes allotted for the run. At a fixed concentration of std, it was discovered that the RP-HPLC method's linearity window was between 10 g ml-1 to 50 g ml-1. The use of the UV spectroscopic method was demonstrated to have a between 100 and 250 g linearity ml-1. Both strategies had regression coefficients (r2) that were higher than 0.999 it was discovered that the thresholds for quantification and detection of RMZ were 1.0 g ml-1 and 3.5 g ml-1, respectively. Remogliflozin etabonate (RMZ) has been determined using straightforward, unique, further more to selective RP-HPLC, ultraviolet (UV), and liquid chromatography spectroscopy procedures that have been created and improved. The primary peak and internal standard peak were individually eluted using various retention durations (RT) in the HPLC technique [44].

**Swapnil Suresh Mankar et al. (2021)**

Tests for the system's applicability, reproducibility, precision (day and night/interval), linearity and calibration, robustness, force degradation, specificity, and drug recovery and accuracy studies are used to test the method's suitability and validate it for solid dosage form estimation of diabetes medications using RP-HPLC results: in accordance with each criteria, remogliflozin's performance met all standards for system appropriateness, including those for factors for tailings (t), separations, theoretical plates (n), capacity (k'), resolution (r), and RSD (%); the verified stress breakdown investigations for remogliflozin under heat, oxidative, alkaline, and acidic circumstances in a few breakdown products (rem) [45].

**Dr. Srinivasan et. al. (2020)**

Remogliflozin and ertugliflozin are estimated using UV, RP-UPLC, RP-HPLC, and LC-MS methods. There are numerous previously published articles that describe analytical methodologies and similar approach validation, the established levels of remogliflozin and ertugliflozin in its pharmaceutical preparations and biological matrices are accounted for by the disclosed analytical procedures that are detailed in the current review. The most popular approaches, including spectrometric and liquid chromatographic procedures, are outlined in this article. Remogliflozin and ertugliflozin HPLC procedures take into account factors like the matrix, composition of the stationary and mobile phases, detection wavelength, and others for remogliflozin and ertugliflozin both separately and together, spectrometric methods incorporate variables like max, solvent, matrix, etc., variables used in HPTLC procedures include combinations of rf, stationary phase, and mobile phase. Additionally, this review gives thorough details on how remogliflozin and ertugliflozin separate when used separately, in combination with other medications, and when their breakdown products are present. There have been reported Remogliflozin and Ertugliflozin determination techniques [46].

**Vashi Dhara et al. (2022)**

Isocratic mode methodology was used to perform the RP-HPLC process on a column of reversed-phase Cosmosil C18 (250 mm, 4.6 mm, 5 i.d.). Acetonitrile made up 60:40% of the mobile phase by volume and water, with a 1 ml/min flow rate, 210 nm detector wavelength was employed. Vildagliptin and remogliflozin etabonate had average retention durations of 3.29 and 5.64 minutes, respectively. The calibration curves for vildagliptin and remogliflozin etabonate were linear (r2>0.999) for between 5-80 g/ml and 10-80 g/ml in terms of concentration, respectively vildagliptin and remogliflozin etabonate both had LODs of 0.010 g/ml and 0.029 g/ml and, correspondingly, LOQs of 0.031 g/ml and 0.088 g/ml. The measurement of Pharmaceutical dose type of Vildagliptin with Remogliflozin Etabonate, an easy, sensitive, verified, specific, and accurate Chromatography RP-HPLC method has been developed [47].

**Amit Chaudhary et al. (2022)**

With the use of a C18 (250 mm 4.6 mm, i.d. 2.5 m) column and isocratic elution, the separation was accomplished. The separation of the analytes employed acetonitrile and 20 mm ammonium formate buffer (PH 3.5) combined at a 60:40 ratio with a flow rate of 1 ml/minute as the stage of mobility. At a wavelength of 243 nm, a diode array detector was used to monitor the segregated effluents. For remogliflozin and met, respectively, the results revealed satisfactory linearity. Additionally, the typical % assessment of commercially available compositions of met as well as remogliflozin turned out to be 100.52% and 100.30%. LOD and LOQ for remogliflozinis 0.42 and 1.28 g ml-1, respectively, while these values are 1.97 gml-1 and 5.96 g ml-1 for met. The suggested approach's selectivity, precision, linearity, and accuracy were all verified. There were no validation parameters outside of the permitted range [48].

**Mahesh Attimarad et al. (2020)**

Utilizing a monolithic c18 column and full factorial box-Behnken design model, under ideal chromatographic circumstances, MFH and RGE were separated by chromatography. The basis for the spectroscopic method was the peak UV spectral intensity of the second-order derivative at zero crossings. Additionally; this is an attempt used for the simultaneous estimate in laboratory-based mixed solutions and formulations of MFH and RGE. Out of 47 possibilities, the final chromatographic condition was selected. Recommended Plots of perturbations, response surface models, and the desirability function demonstrated the impact of the Chromatographic specifications. Additionally, the RGE and MFH HPLC methods both shown high linearity in the range by using spectroscopic and HPLC methods. Average percent assay for MFH and RGE, respectively, yielded results of 99.51% and 99.80% and 99.60% and 100.07%. Remogliflozin as well as metformin in dosage form was effectively determined using this approach, with acceptable recoveries [49].

**Mahesh Attimarad et al 2022**

Three variables, acetonitrile, ethanol, and water, interact and have a quadratic impact. Percentage, movable stage, pH, and the resolution of the flow rate between the peaks were optimised using the box-Behnken

approach and response surface design. The desirable function design space was utilised to identify the ideal chromatographic environment in order to predict the Resolution of the three anti-diabetic medications' peaks (2.7 and 6.5) the isocratic elution method, which employed Acetonitrile and phosphate buffer (20 mm kh2po4, pH adjusted to 4.9 with orthophosphoric acid) were applied over a zorabx c18 HPLC column at a ratio of 58:42, successfully separated all three analytes in 2.5 minutes. Additionally, recommendations were used to validate the optimised HPLC process. The low percent relative standard deviation (0.60-1.65%), good percentage recovery (98.18-101.50%), and low percent (0.20-1.82%) relative errors provided evidence for the precision and accuracy of the developed HPLC method. By gently changing the five various parameters, the resilience of the method was also shown [50].

**Shivani v. Trivedi et al. (2021)**

In order to measure metformin HCL and remogliflozin etabonate simultaneously are in their synthetic mixture. There was developed a reverse phase high performance liquid chromatographic technique created by using a cosmosil c18 column (250 mm x 4.6 mm, 5 m) methanol (60:40) as the mobile phase, flowing at a rate of 1 ml/min, and buffer (pH 4.0), the separation was accomplished. The detection wavelength was 241 nm. It was discovered that metformin HCL and remogliflozin etabonate have retention times of 5.493 minutes and 3.183 minutes, respectively. Linearity, accuracy, and precision have all been verified for the approach. 5–15 g/ml of remogliflozin etabonate and 20–60 g/ml of metformin HCL both showed linearity. This approach was created with the goal of simultaneously estimating the remogliflozin and metformin in bulk and commercial dose forms [51].

**UV -Spectroscopic**

Spectrophotometry, another name for UV-vis spectroscopy, is a quantitative technique for determining how much light each particular molecule absorbs. In order to do this, the amount of light passing through a sample is compared to the amount of light passing through a reference sample or a blank. Glass, liquids, solids, thin films, and other sample types can all be analysed using this method.

**Attimarad Mahesh et al. (2022)**

In order to establish two processed UV spectrophotometric approaches, the peak amplitude at zero-crossing of second derivative spectra ofanalytes. The second approach is creating zero-order spectra from a mixture of analyte spectra by multiplying and dividing them by the spectra of the pure analyte in order to cancel out the influence of one of the analytes. Results: for RGF and VGT, respectively, both methods demonstrated linearity concentrations in the range of 2-75 g/ml and 2-50 g/ml. Low LOD and LOQ values discovered for RGF and VGT by both approaches demonstrated the methods' high sensitivity. For RGF and VGT, respectively, the mean percentage recovery was 98.60% and 100.78%, and both had low relative error percentages of 98.81% and 99.15%. The results were compared to the reported techniques for the assay of the VGT and RGF from the drug [52].

**HPTLC method**

HPTLC (high-performance thin-layer chromatography), a development of thin layer chromatography (TLC), is a reliable, easy-to-use, quick, and effective technique for quantitative analysis of substances. An analytical method called HPTLC is based on traditional liquid chromatography (TLC), but it has been improved to allow for quantitative analysis of the compounds and to improve the separation of the compounds' resolution. Some of the improvements allow for better resolution, such as when higher-quality TLC plates are used, which have finer stationary phase particle sizes. Using a multiple development apparatus, the plate can be developed again to further increase the separation. Consequently, HPTLC delivers higher resolution and a lower limit of detection (LOD’s) [53].

**Reema Jaiswal et al. (2022)**

On a precoated silica gel aluminium plate 60f254 (20 x 10) 100 m thick, the medicines were separated by chromatography, with the mobile phase being a mixture of methanol, ethyl acetate, and acetic acid (6:3.5:0.5v/v). The TLC scanner was tuned at 245 nm. 0.23 rf values for met and 0.83 for remogliflozin, respectively, indicate that the two medicines were satisfactorily resolved. Remogliflozin etabonate and metformin hydrochloride had polynomial calibration curves in the 200–1200ng/band and 1000–6000ng/band concentration ranges, respectively. The values for the Metformin has correlation values (r) of 0.9999 and 0.9999 etabonate and hydrochloride, respectively, of remogliflozin. The suggested method is accurate and resilient, as evidenced by the both with a modest relative standard deviation (2%) the studies on precision and robustness. The approach obtained a 98.82% accuracy rate for metformin hydrochloride and 98.42% for remogliflozin etabonate were approved in accordance with regulatory regulations. They came to the conclusion this experiment that the newly created approach for simultaneously estimating the remogliflozin and

metformin hydrochloride discovered towards straightforward, accurate, exact, high resolution, with time-efficient which made this technique extra palatable and economical [54].

**DimalA. Shah et al. (2021)**

The stationary phase was a mixture of methanol, ethyl acetate, toluene, and nh3 (2:4:4:0.1, v/v/v) on HPTLC plates coated with silica gel 60 f254 was utilized as the mobile phase, and densitometry was employed to quantify the drug's estimate. The suggested approach was tested prior to usage, for durability, linearity, accuracy, and precision estimate the dosage of a medicine in tablet form Remogliflozin etabonate was found to have a RF value of 0.61 at 229 nm, the reflectance mode was used to carry out the densitometric estimation. For remogliflozin etabonate, the technique was discovered to be linear in the 500–8000 ng/band range by conducting tests on forced degradation, the potential degradation pathway was estimated. With respect to their rf value, The deteriorating summits were satisfactorily separated since the drug peak. The newly created HPLC technique was easy, quick, accurate, and precise. Therefore, the technique can be effectively applied to the study of the pharmaceutical industry use of remogliflozin etabonate [55].

**UPLC and RP-UPLC**

UPLC is a novel class of separation technology that makes use of sub-2 m particles for the stationary phase and is based on established liquid chromatography concepts. The clarity and sensitivity, and analysis rapidity of these particles have dramatically increased due to their high mobile phase linear velocities. This approach has received a lot of interest recently for pharmaceutical and biomedical analysis due to its speed and sensitivity [56].

**Ali, s. m. et al. (2021)**

A new kind of separation is known as UPLC method that makes use for the stationary phase, of sub-2 m particles and is based on well-known liquid chromatography principles 0.1 m acetate buffer at PH 5.7 and a ratio of 25:75 (v/v) methanol at a flow rate of 0.3 ml/min with a PDA detector operating at 215 nm under these circumstances, the compounds' it was resolved measured at 12.57, with remogliflozin's retention duration being 2.67 minutes, compared to 3.84 minutes for vildagliptin. The technique's applicability for the system, scope of analysis, accuracy, specificity, stability, and robustness were all confirmed. The analytes were subjected to five distinct stress conditions throughout the forced degradation investigation, and the overall degradation condition. The approach can separate and measure the amounts of vildagliptin and remogliflozin in pharmaceutical formulations, and the percentage of degradation was very low [57].

**V.A. Patel et al. (2021)**

The goal of this project is to simultaneously create quick and easy RP-UHPLC methods for quantifying remogliflozin. Remogliflozin and met were separated by chromatography using acetonitrile: phosphate buffer (PH: 3) (60:40%, v/v) on a zorbax eclipse plus c18 (1504.6 mm, 5 m) column. Mobile phase, a diode array detector, and a flow rate of 1.0 ml/min at 230 nm. Remogliflozin had an average percent assay of 99.51%, whereas met had an average percent assay of 99.60%. The outcomes of the retrieval studies conducted validate the projected process's high degree of accuracy. The devised chromatographic approach can therefore be effectively used for estimate of metformin and remogliflozin in their formulation and bulk. It is accurate, precise, and selective [58].

**LC-MS method**

In the LC-MS analytical procedure, target chemicals (or analytes) are physically separated before being detected by mass spectrometry despite being a relatively new technology, it has quickly gained popularity for its ability to detect various analytes in microgram or even nanogram concentrations, such as insecticides, food additives, medication metabolites, and natural product extracts.

Application of LC-MS /MS:

1. The measurement of genotoxic contaminants in pharmaceutical active ingredients [59].
2. Measurement of drug metabolites in bodily fluids.
3. Bacterial cell quantitation of nucleotides and their derivatives [60].

**Sai Prudhvi n. et al. (2021)**

In the therapy of type II diabetes in human plasma, remogliflozin and vildagliptin are utilized. Liquid-liquid extraction was used to separate the analytes from the spiked plasma matrix and choose the medication analogliptin as the internal standard and the extracts underwent chromatographic analysis on an in ertsilods (4.6 mm100 mm, 5 m) C18 column. The mobile phase contains methanol, acetonitrile, and 0.1% formic acid in a ratio of 40:50:10 (v/v) at a flow rate of 0.5 ml/min. The analysis was finished in 6 minutes. The technique generates peaks at 2.6 min for remogliflozin etabonate, 2.7 min for vildagliptin, and 1.2 min for alogliptin with adequate symmetry and resolution with satisfactory system compatibility (internal standard).

The characteristic fragment ion transitions for remogliflozin and vildagliptin at m/z 523 to m/z 247 and 304 to m/z 180, respectively, are confirmed by mass spectral analyses. The technique has a lower LOQ of 5 ng/ml and can identify analytes upto1.5 ng/ml. it has a wide calibration range of LOQ to 300 ng/ml &HQC (high quality control concentration) levels and generate findings that are suitable. Remogliflozin and vildagliptin multiplexed quantification techniques have been designed and validated using sensitive, specific, and dynamic LC-MS/MS assay. The presented techniques can handle significant research trials with enough through put.

**Dr. Satyadev et al. (2022)**

This article reviews current developments in bioanalytical lc-ms/ms techniques for utilising water sx bridge c18 column (150x4.6 mm, 3.5) and 70:30 ratio's organic mobile phase, combine acetonitrile and sodium dihydrogen phosphate. In the case of remogliflozin, the calibration curve was linear at 350ng/ml. Results for stability, matrix effect, accuracy, recovery, and precision were determined to be within acceptable bounds. In pharmacokinetic investigations, a quick and effective method for observing the examined analytic and was created.

## *Conclusion*

This review article discusses the remogliflozin's physiological characteristics, drug profile, and clinical studies including safety and efficacy and adverse effect of a drug. The review that is being presented provides on the many approaches that have been used to identify remogliflozin and its ester form. This review conclusion that many analytical techniques, including RP-HPLC, UV, HPTLC, RP-UPLC, LC-MSmethod have been described for estimating remogliflozin alone and its combinations. Thus, these techniques were discovered to be straightforward, precise, economical, and repeatable in nature because RP-HPLC and RP-UPLC offered the best available reliability, repeatability, analysis time, and sensitivity, these techniques were used for the majority of procedures. The developed RP-HPLC and RP-UPLC chromatographic conditions are used in a method for the simultaneous measurement of singles and their combination is quick, accurate, precise, and simple, and it may be used in laboratories for standard quality control tests on both formulations.

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## Адамдардағы 2-типті қант диабетін емдеуде SGLT-2 ремоглифлозин ингибиторына шолу

Натрий-глюкоза тасымалдау ақуызы 2 ингибиторлары, әсіресе жүрек немесе бүйрек аурулары бар адамдарда, 2-типті қант диабетін емдеуге арналған пероральды дәрі-дәрмектердің маңызды санатына айналды және жалпы заманауи зерттеулердің жоғары бағасына ие болды. Олар қан қысымын төмендетіп, адамдарға салмақ жоғалтуға көмектеседі, бірақ олардың кемшілігі бар, атап айтсақ, несепжыныс жүйесінің инфекциясын тудырады. Ремоглифлозиннің жаңадан мақұлданған комбинациясы — бұл жаңа фармацевтикалық класс пен қант диабетін емдеуге арналған препараттардың жаңа комбинациясын зерттеу. Ремоглифлозин этабонаты — ремоглифлозиннің эфирлік түріне арналған термин. Бұл шолуда ремоглифлозин этабонатының клиникалық тиімділігі, қауіпсіздік профилі, фармакокинетикасы және фармакодинамикасы зерттелген. Алайда, оны RP-HPLC, UV, RP-UPLC, HPTLC және LC/MS көмегімен аналитикалық профильдеу қажет. Авторлар ремоглифлозин этабонатының аналитикалық әдісін әзірлеу кезінде жүргізілген жеке эксперименттерді қарастырған.

*Кілт сөздер*: ремоглифлозин этабонаты, SGLT-2 ингибиторы, 2-типті қант диабеті, аналитикалық әдіс.

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## Обзор ингибитора SGLT–2 ремоглифлозина в лечении сахарного диабета 2-го типа у человека

Ингибиторы натрий-глюкозного транспортного белка 2 стали значительной категорией пероральных препаратов для лечения сахарного диабета 2-го типа, особенно у людей с заболеваниями сердца или почек, и, в целом, получили высокую оценку современных исследователей. Они могут снижать артериальное давление и помогают людям в процессе снижения веса, однако у них есть и недостатки, например, инфекции мочеполовой системы. Недавно одобренная комбинация ремоглифлозина — это исследование нового фармацевтического класса и новой комбинации препаратов для лечения диабета. «Ремоглифлозин этабонат» — термин, обозначающий эфирную форму ремоглифлозина. В настоящем обзоре изучены клиническая эффективность, профиль безопасности, фармакокинетика и фармакодинамика ремоглифлозина этабоната, но его аналитическое профилирование производится с использованием RP-HPLC, UV, RP-UPLC, HPTLC и LC/MS. Авторами рассмотрены отдельные эксперименты, проведенные при разработке аналитического метода для ремоглифлозина этабоната.

*Ключевые слова*: ремоглифлозин этабонат, ингибитор SGLT–2, сахарный диабет 2-го типа, аналитический метод.