مجلة الدراسات التربوية والعلمية - كلية التربية - الجامعة العراقية
العدد الثالث والعشرون - المجلد الخامس - علوم الكيمياء - آيار 2024 م
doi.org/10.52866/esj.2023.05.23.08

HPLC techniques for quantifying glimepiride in pharmaceutical preparations and human samples: A review

Ali Amer Waheb [1], Mustafa J. Mohammed[2], and Ashraf Saad Rasheed[3]
[1] Department of Chemistry, College of Science, Mustansiriyah University, Baghdad, Iraq
[2] Department of Chemistry, College of Education, Al-Iraqia University, Baghdad, Iraq.
[3] Department of Chemistry, College of Science, University of Baghdad, Baghdad, Iraq

Abstract:

Type 2 diabetes has become a global epidemic impacting approximately 190 million individuals globally with an expected increase to over 300 million by 2025. The influence of diabetes on individual health, healthcare, and society as a whole is significant and ongoing. Due to the significance of this oral hypoglycemic agent in managing type 2 diabetes, it works by stimulating insulin secretions from beta cells in the pancreas and is also known to enhance peripheral insulin sensitivity and thus reduce insulin resistance. Glimepiride is an antidiabetic drug that features both hydrophilic and hydrophilic functional groups in its molecular composition. Glimepiride has a strong ability to contaminate water bodies. Being a drug that pollutes the environment, there is an urgent need for this. A review of analytical work reported in the literature on pharmaceutical preparations and human samples using various techniques such as spectrophotometry, electrochemical techniques, capillary electrophoresis, and HPLC.

Keywords: Antidiabetic drug, Glimepiride, HPLC, and pharmaceutical preparations.

تقنيات كروموتوغرافيا السائل عالي الاداء لتقديردواء الجليميبريد تقدير كميا في المستحضرات الصيدلانية والعينات البشرية : مراجعة

علي عامر وهيب[1] , مصطفى جاسم محمد[2] , أشرف سعد رشيد[3]
[1] قسم الكيمياء, كلية العلوم, الجامعة المستنصرية , بغداد, العراق
[2] قسم الكيمياء , كلية التربية , الجامعة العراقية , بغداد,العراق
[3] قسم الكيمياء , كلية العلوم, جامعة بغداد, بغداد, العراق

مستخلص

حوالي 190 مليون شخص حول العالم يعانون من مرض السكري من النوع الثاني وهناك توقعات بان تحدث زيادة في الاصابات لتصل الى اكثر من 300 مليون شخص بحلول عام 2025 . تأثير مرض السكري على صحة الأفراد، والرعاية الصحية، والمجتمع بشكل عام يظل بارزًا ومستمرًا. جليميبريد هو دواء مضاد لمرض السكري يتميز بوجود مجموعات وظيفية محبة وكارهه للماء في تركيبته الجزيئية. نظرًا لأهمية هذا العامل المخفض لسكر الدم عن طريق الفم في إدارة مرض السكري من النوع الثاني، فإنه يعمل عن طريق تحفيز إفراز الأنسولين من خلايا بيتا في البنكرياس، ومن المعروف أيضًا أنه يعزز حساسية الأنسولين في الأنسجة المحيطية وبالتالي يقلل من مقاومة الأنسولين .يتمتع الجليميبريد بقدرة قوية على التلوث للمياه الجوفية، وبوصفه دواءًا يسبب تلويثاً للبيئة، هناك حاجة ملحة لمعالجة هذه المسألة. يتضمن هذا البحث استعراض للدراسات المذكورة بالادبيات حول تقدير دواء الجليميبريد في المستحضرات الصيدلانية وعينات بشرية بأستخدام تقنيات متنوعة مثل تقنية الطيف الضوئي والتقنيات الكهروكيميائية والترحيل الكهربائي وكروموتوغرافيا السائل عالي الاداء.

الكلمات المفتاحية : دواء مضاد لمرض السكر، جليميبريد، كروموتوغرافيا السائل عالي الاداء، المستحضرات الصيدلانية .

Introduction:

Glimepiride (GLM) is its scientific name 3-ethyl-4-methyl-N-(4-(N-((4- methylcyclohexyl) carbamoyl) sulfamoyl)phenethyl)-2-oxo-2,5-dihydro-1H-pyrrole-1-carboxamide[1]. The molecular formula for this drug is $C_{24}H_{34}N_4O_5S$, with a molecular weight of (490.62g/mol) [2] GLM is not related to insulin (Insulin Independent) and it is from the second generation of a group of sulphonylureas, and one of its advantages is that it leads to lowering the amount of sugar in the blood more effectively than the old drugs, which are considered from the first generation, such as Tolbutamide and Chlorpropamide. This drug helps to secrete insulin from the cells of the pancreas and helps to transport sugar in the blood into the tissues of the body. The use of this medicine must be combined with a diet. GLM has a long duration of drug efficacy, which extends to 24 hours, so it is taken once a day [3].GLM is a white crystalline powder with a bitter taste [4]. The percentage of elements is C = 58.76%, H = 6.99%, O=16.30%, N=11.42%, and S = 6.53% [5] .It dissolves in alcohol at 25 °C and is slightly soluble in water. And a melting point of 207 C °. The maximum absorption wavelength is (229-260) nm [6] This medicine is available in the form of different pharmaceutical preparations. This drug has side effects, including severe skin rash, itching, redness, irritation, pale skin, fever, general weakness, and numbness. Or feeling tingling, difficulty breathing, dizziness, headache, fatigue, vomiting, stomach pain, nausea, diarrhea, enhanced sensitivity of the skin to sunlight, mild itching [7, 8] This drug has interactions that may cause a reaction similar to disulfiram (facial redness, headache, shortness of breath), as well as androgens, methyldopa, magnesium salts, chloramphenicol, fluconazole, antihistamines, sulfonamides, nicotinic acid, minotiazine, rifamycin, estrogen, isoniazid. These drugs cause high blood sugar and thus reduce the control of sugar. Fluconazole, fluvastatin, flavoxamine, and ketoconazole may increase the levels of glimepiride in the blood and increase the risk of hypoglycaemia [9,10] The structure of glimepiride is shown in **Figure 1.**

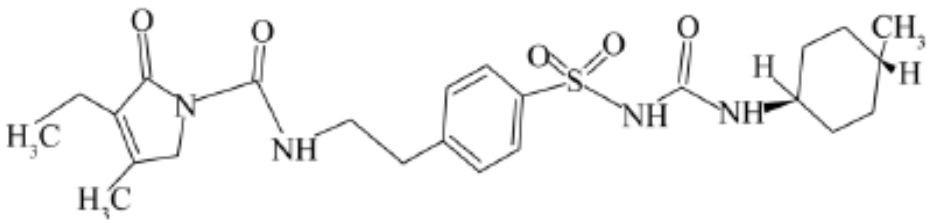

Figure 1. Chemical structures of glimepiride

The drug GLM was determined by various methods, including ultraviolet spectroscopy, where the scientist Altinoz and his group [11] were able to analyze the drug GLM using the spectrophotometry of the derivative The second is for ultraviolet rays, where quantitative spectrophotometry was conducted in dimethyl in the wavelength from 245nm to 290 nm, where it appeared at (236.3-268.2) nm, respectively. Dhaneshwar and his group [12] validated the HPTLC technique was employed for the determination of atorvastatin and GLM in pharmaceuticals and preparations, namely: A new, simple, and accurate method for the simultaneous determination of drugs for both ATV and GML in tablet form, where the drug was carried out on precoated aluminum plates utilizing silica as a stationary phase and an eluent consisting of H_2O, MeOH and ammonium sulfate in proportions (4:1:1) respectively.

GLM was quantified by the micellar electrokinetic chromatography (MEKC) technique [13]. A method based on switching the polarity of the reverse electrode was used to determine Serum antihyperglycemic drugs after ACN protein precipitation. The detection limit is (3.1 µmol $.L^{-1}$), (%Recovery(%rec) = 93%). GLM was determined by LC-ESI-MS-MS [14] to analyze human plasma samples for drug applications. The evidence obtained has a glimepiride retention time of 1.65 min and a concentration range of (5-1000 $ng.ml^{-1}$). GLM was determined in pharmaceutical preparations by the square wave Voltammetric Method [15]. Where the cyclic voltammetry technique was employed to investigate the electrochemical behaviour of GLM. The peak current detected was positively related to the concentration of GLM. Evidence obtained at a linearity in the range (0.25-7.81 µg ml^{-1}). The accuracy of the suggested

technique was confirmed by the %rec of 100.95 ± 0.61% with RSD = 1.4% at the concentration level is 4.89 µg ml $^{-1}$.

Maurer and his group [16] presented a rapid and reliable examination and determination in addition to the accurate and sensitive quantitative measurement of oral antidiabetics GLM by the technique of APCI-LC-MS In plasma allowing determination of overdose, evidence obtained (LOD = 0.01mg/1) and (LOQ=0.1mg/1).

GLM was determined using liquid-liquid extraction (LLE) [17 Where it proved to be a sensitive and specific method for the drug at a linear concentration (2 -500 ng ml-1).

Determination of GLM using HPLC based analytical methods offers lower time requirements, less use of organic solvents, and better separation and determination of GLM, which are presented in (Table 1).

Table 1: HPLC methods for determining GLM in human samples and pharmaceutical preparations.

Column	Mobile phase	Detection	Statistical data analysis	Application	Ref.
C18	0.05 M $HClO_4$: ACN (60: 40 v/v)	UV λ:350 nm	6-1000 ng ml^{-1} t_r= 3.5 min LOD= 5 ng ml^{-1}	human serum and urine	[18]
C8	ACN: NH_4OAc (pH 3.0; 0.02M) (20:80, v/v)	UV-DAD **λ**:235 nm and mass spectrometry	Fragment ions 376.2455 (376.0967)	Bulk drug substance	[19]
C18	ACN:0.005 mol/ NH_4OAc (60:40)	ESI-MS-MS	0.1-200 ng ml^{-1} LOQ= 5 ng ml^{-1} %RSD= 0.50-5.8 %Rec = 79.8	Human plasma	[20]
Lichrosorb®	ACN: H2O – CH_3COOH (550:450:0.6 v/v)	UV **λ**:350 nm	15-120 µg/mL LOD = 4 ng/ µg LOQ = 10 ng /µg %RSD = 0.521 %Rec = 99.34	Pharmaceutical formulations	[21]
C18	NH_4OAc buffer (0.02 mol) ACN: MeOH (40:35:25 v/v)	ESI-MS-MS	5-500 ng/mL r^2= 0.9998 LLOQ = 5.0 ng/ml % precision= 7.96 % Accuracy=100.58	Human plasma	[22]

Column	Mobile phase	Detection	Statistical data analysis	Application	Ref.
Hypersil ODS	HCOOH 0.05M: ACN (28:72 v/v)	ESI-MS-MS	0.50-1000 ng/mL r^2= 0.998 LOD = 0.16 ng/mL LLOQ = 0.75 ng/ml %RSD= 10.37	Human plasma	[23]
Hypurity C18	ACN :1 g/L HCOOH in H_2O (50:50 v/v)	ESI-MS-MS	15.6-1000 µg/mL r^2= 0.990 LOD = 0.98 µg/mL LOQ = 15.6 µg/mL	Human plasma	[24]
Peerless Basic C18	MeOH and H_2O Including 0.5% HCOOH) 80:20 v/v	ESI-MS-MS	10-1500 ng/mL t_r = 4.5 min r^2= 0.99 LLOQ = 2.50 ng/ml % Accuracy= 92.81 %Recovery = 93	Human plasma	[25]
Capcell Pak MF Ph-1	ACN: 0.01 mol/L PO_4 buffer (20:80, v/v) Including 0.04% of Et3N	UV **λ**:228 nm	10-400 ng/mL t_r= 4.5 min r^2= 0.9997 LOQ = 10 ng/ml % precision= 15 % Accuracy=99	Human plasma	[26]
C18	ACN: H2O Including 1% Et3N (pH was adjusted to 5.6 with H_3PO4) (55:45 v/v)	UV **λ**:230 nm	1-1600 ng/mL t_r = 9.8 min r^2= 0.998 LOD = 0.75 ng/mL LLOQ = 1 ng/mL % Accuracy= 105 %Recovery = 96	Human plasma	[27]
C18	ACN: 2% HCOOH pH 3.5 (80:20 v/v)	UV **λ**:228 nm	20-140 ng/mL %RSD= 0.62 %Recovery = 100.20	Tablets	[28]
phenomenex RP-18	ACN: PO_4 buffer (65: 35)	UV **λ**:228 nm	0.25-25 µg/mL t_r = 8.7min r^2= 0.9991 LOD = 0.058 µg/mL LOQ = 0.20 µg/mL	Tablets	[29]

Column	Mobile phase	Detection	Statistical data analysis	Application	Ref.
C18	ACN: PO_4 buffer (48:52, v/v)	UV **λ**:228 nm	20-300 µg/mL r^2= 0.999 %RSD= 0.297 %Recovery = 102.678	Bulk drug substance	[30]
Cosmosil C18	0.01 mol $(NH_4)_3C_6H_5O_7$ (pH 6.95): ACN: MeOH (45:35:20 v/v)	UV **λ**:228 nm	0.10-10.00 µg/mL t_r = 5.6min r^2= 0.9999 LOQ = 0.02 µg/mL %RSD= 0.6 % Accuracy= 99.7	Tablets	[31]
Agilent Zorbax XDB C18	aqueous buffer: ACN (68:32 v/v)	UV **λ**:228 nm	0.1-0.6 µg/mL t_r = 8.1 min LOD = 0.007 µg/mL LOQ = 0.022 µg/mL %RSD= 1.16	Tablets	[32]
Waters Symmetry	H_2O and THF (75:25 v/v)	UV **λ**: 228 nm	600-6000 mg /mL t_r = 0.6 min r^2= 0.998 LOD = 200 mg /mL LOQ = 600 mg /mL %RSD= 0.6	Bulk drug substance	[33]
Phenomenex Luna C8	PO_4 buffer: ACN: THF (73:18:09, v/v/v)	UV **λ**:228 nm	600-6000 µg/mL t_r = 41 min r^2= 0.999 LOD = 0.02µg/mL LOQ = 0.04 µg/mL %RSD= 1.13 % Accuracy= 110	Bulk drug substance	[34]
Inertsil-ODS-3 (C-18)	composed of MeOH:PO_4 buffer (75:25 v/v)	UV- DAD **λ**:258 nm	1-10 µg/mL t_r= 10 min r^2= 0.999 %RSD= 0.64 %Rec = 100.2	Tablets	[35]
Alltima C18	MeOH:PO4 buffer (70:30, v/v)	UV **λ**: 230 nm	1-100 µg/mL r^2= 0.99992 LOD = 0.26µg/mL LOQ = 0.88 µg/mL %RSD= 0.20 % Accuracy= 100.40	Tablets and dietary	[36]

Column	Mobile phase	Detection	Statistical data analysis	Application	Ref.
GraceSmart RP-18	35% A (90% H_2O: 0.1% HCOOH:10% ACN) and 65% B (90% ACN: 10% H_2O)	UV detection at 210 nm	10-90 µg/mL r^2= 0.99 LOD = 27 ng/µg %Recovery = 91.0 % Accuracy= 98.6	Dietary supplements and tablets	[37]
Alltima HP C18	ACN: 10 mM NH_4OAc (pH 3.0) 60:40(v/v)	LC-MS/MS	4.98-494.2 ng/mL r^2= 0.99 LLOQ =4.97 ng/mL % Accuracy= 99.28	Human plasma	[38]
C18	0.001M NaH_2PO_4: 10% H_3PO_4: ACN	UV **λ**:228 nm	40-140 µg/mL t_r =9.3 min r^2= 0.998 LOD = 0.354 µg/mL LOQ = 1.18 µg/mL %RSD= 0.21 % Accuracy= 99.96	Bulk and Tablet Dosage Form	[39]
octadesyl silane (ODS) column	ACN, 0.2 M PO_4 buffer (pH 7.4) (40:60 v/v)	PDA **λ**:228 nm	0.2-2 µg/mL t_r =3.54min r^2= 0.999 LOD = 0.38 µg/mL LOQ = 1.17 µg/mL %RSD= 0.127 %Rec = 99.87	pharmaceutical formulations and in vitro dissolution studies.	[40]
Kine-tex C18 fused-core	ACN: K_2HPO_4 10 mM pH 3.0 (60:40v/v)	UV **λ**: 230 nm	0.1-1.0 µg/mL t_r =1.8min r^2= 0.9957 LLOQ =5.1 µg/mL %RSD= 3.25	Human plasma	[41]
HILIC Waters Spherisorb S5NH2	40% ACN:60% aqueous CH3COO buffer (5.0 mM) at pH 6.3 (40:60v/v)	UV **λ**:228 nm	50 µg/mL-6mg/L t_r =5min r^2= **0**.999 LOD = 15 µg/mL %RSD= 0.84 %Rec = 99.87	pharmaceutical formulations	[42]

RSD: Relative Standard Deviation; LOD: Limit of Detection; LOQ: Limit of Quantitation; LLOQ: Lower Limit of Quantification; DAD : diode array detector; PDA: photo diode array ,perchloric acid: $HClO_4$; ammonium acetate: NH_4OAc; glacial acetic acid: CH_3COOH ; formic acid: HCOOH ; phosphate:PO_4 ; triethylamine: Et_3N ; orthophosphoric acid: H_3PO4 ; triammonium citrate: $(NH_4)_3C_6H_5O_7$; tetrahydrofuran :THF ; monobasic sodium phosphate: NaH_2PO_4 ; potassium phosphate: K_2HPO_4 ; acetate : $CH3COO^-$, Methanol ; MeOH.

Conclusion:

The analysis of glimepiride should be straightforward, fast, and cost-effective. glimepiride in pharmaceutical formulations by HPLC with UV detection showed to be an adequate technique due to this technique offering accurate results at a lower cost compared to more complex detection methods. Moreover, the developed methods enabled the concentration of the glimepiride drugs in the sample matrix without the need for an additional step.

Reference:

[1] **"U.S.Pharmacopeia on CD-ROM",**30th Ed .NF25,by system simulation 1td. The stationary office , America,3071,**(2007).**

[2] Glimepiride- **"Drugs.com. All rights reserved"., (2013)**

[3] **Glimepiride-"DrugBank version 4.0 beta is now online for public preview".**

[4] **"British Pharmacopeia on CD-ROM**",vol(1,2) **.(2006).**

[5] Glimepiride-**"Digital Media Services".,(2013).**

[6] Amaryl-**"Digital Media Services".,(2013).**

[7] Glimepiride side effects-**"Medical Dictionary All Rights Reserved"**

[8] Glimepiride-**"Medical Dictionary All Rights Reserved"**

[9] dms@choueirigroup.com.

[10] P.J.Neuvonen, M.Niemi and J.T.Backman., perspectives in clinical pharmacology ." **J.of clinical pharmacology and Therapeutics".,** 80 , 565-581**, (2006).**

[11] S. Altino 2 and D. Tekeli ., Analysis of Glimepiride by Using derivative spectrop **." J . of pharmaceutical and Biomedical Analysis" .,** 24 , 3 , 507-515**, (2001) .**

[12]S. R. Dhaneshwar , J. V . salunkhe , and V . K . Bhusiri ., Validated HPLC Method for simultaneous Estimation of metformine Hydrochloride , Atorvastatin and Glimepiride in Bulk Drug and formulation . **"J. of Analytical and Bio analytical Techniques "., 1,109, (2010)** .

[13] V. Maier, J. Znaleziona, D. Jirovský, J. Skopalová, J. Petr, and J. Ševčík, "Determination of antihyperglycemic drugs in nanomolar concentration levels by micellar electrokinetic chromatography with non-ionic surfactant," *J. Chromatogr. A*, vol. 1216, no. 20, pp. 4492–4498, 2009.

[14]N. Yüzüak, T. Özden, S. Eren, and S. Özilhan, "Determination of glimepiride in human plasma by LC-MS-MS," *Chromatographia*, vol. 66, no. SUPPL. 1, pp. 165–168, 2007.

[15]I. Suslu and S. Altinoz, "Determination of Glimepiride in Pharmaceutical Formulations by Square-Wave Voltammetric Method," *Curr. Anal. Chem.*, vol. 7, no. 4, pp. 333–340, 2011.

[16]H. H. Maurer, C. Kratzsch, T. Kraemer, F. T. Peters, and A. A. Weber, "Screening, library-assisted identification and validated quantification of oral antidiabetics of the sulfonylurea-type in plasma by atmospheric pressure chemical ionization liquid chromatography-mass spectrometry," *J. Chromatogr. B Anal. Technol. Biomed. Life Sci.*, vol. 773, no. 1, pp. 63–73, 2002.

[17]Y. Dotsikas, C. Kousoulos, G. Tsatsou, and Y. L. Loukas, "Development of a rapid method for the determination of glimepiride in human plasma using liquid-liquid extraction based on 96-well format micro-tubes and liquid chromatography/tandem mass spectrometry," *Rapid Commun. Mass Spectrom.*, vol. 19, no. 14, pp. 2055–2061, 2005.

[18]K. H. Lehr and P. Damm, "Simultaneous determination of the sulphonylurea glimepiride and its metabolites in human serum and urine by high-performance liquid chromatography after pre-column derivatization," *J. Chromatogr. B Biomed. Sci. Appl.*, vol. 526, no. C, pp. 497–505, 1990.

[19]G. Bansal, M. Singh, K. C. Jindal, and S. Singh, "LC-UV-PDA and

LC-MS studies to characterize degradation products of glimepiride," *J. Pharm. Biomed. Anal.*, vol. 48, no. 3, pp. 788–795, 2008.

[20] I. I. Salem, J. Idrees, and J. I. Al Tamimi, "Determination of loratadine in human plasma by liquid chromatography electrospray ionization ion-trap tandem mass spectrometry," *J. Pharm. Biomed. Anal.*, vol. 34, no. 1, pp. 141–151, 2004.

[21] M. Validation and V. Maslarska, "Vania Maslarska," vol. 5, no. 8, pp. 3195–3198, 2014.

[22] I. I. Salem, J. Idrees, and J. I. Al Tamimi, "Determination of glimepiride in human plasma by liquid chromatography- electrospray ionization tandem mass spectrometry," *J. Chromatogr. B Anal. Technol. Biomed. Life Sci.*, vol. 799, no. 1, pp. 103–109, 2004.

[23] C. Pistos, M. Koutsopoulou, and I. Panderi, "Improved liquid chromatographic tandem mass spectrometric determination and pharmacokinetic study of glimepiride in human plasma," *Biomed. Chromatogr.*, vol. 19, no. 5, pp. 394–401, 2005.

[24] G. Hoizey *et al.*, "Identification and quantification of 8 sulfonylureas with clinical toxicology interest by liquid chromatography-ion-trap tandem mass spectrometry and library searching," *Clin. Chem.*, vol. 51, no. 9, pp. 1666–1672, 2005.

[25] P. Sengupta *et al.*, "LC-MS-MS development and validation for simultaneous quantitation of metformin, glimepiride and pioglitazone in human plasma and its application to a bioequivalence study," *Chromatographia*, vol. 69, no. 11–12, pp. 1243–1250, 2009.

[26] Y.-K. Song *et al.*, "Determination of glimepiride in human plasma using semi-microbore high performance liquid chromatography with column-switching," *J. Chromatogr. B*, vol. 810, no. 1, pp. 143–149, 2004.

[27] H. Kotagiri, R. Gannu, C. R. Palem, S. K. Yamsani, V. V. Yamsani, and M. R. Yamsani, "Simultaneous determination of glimepiride and atorvastatin in human serum by high-performance liquid chromatography: Application to pharmacokinetic study," *J. Liq. Chromatogr. Relat. Technol.*, vol. 34, no. 19, pp. 2420–2432, 2011.

[28] I. U. Khan, F. Aslam, M. Ashfaq,

and M. N. Asghar, "Determination of glimepiride in pharmaceutical formulations using HPLC and first-derivative spectrophotometric methods," *J. Anal. Chem.*, vol. 64, no. 2, pp. 171–175, 2009.

[29]"No Title 分子時計によるエネルギー代謝調節," vol. 27, no. 7, pp. 1–5, 2009.

[30]P. Kovaříková, J. Klimeš, J. Dohnal, and L. Tisovská, "HPLC study of glimepiride under hydrolytic stress conditions," *J. Pharm. Biomed. Anal.*, vol. 36, no. 1, pp. 205–209, 2004.

[31]R. T. Sane, S. N. Menon, S. Inamdar, M. Mote, and G. Gundi, "Simultaneous determination of pioglitazone and glimepiride by high-performance liquid chromatography," *Chromatographia*, vol. 59, no. 7–8, pp. 451–453, 2004.

[32]B. L. Kolte, B. B. Raut, A. A. Deo, M. A. Bagool, and D. B. Shinde, "Simultaneous determination of metformin and glimepride in pharmaceutical dosage form by reverse-phase liquid chromatography," *J. Sep. Sci.*, vol. 28, no. 16, pp. 2076–2079, 2005.

[33]D. B. Pathare, A. S. Jadhav, and M. S. Shingare, "RP-LC determination of the cis-isomer of glimepiride in a bulk drug substance," *Chromatographia*, vol. 66, no. 7–8, pp. 639–641, 2007.

[34]M. A. Khan, S. Sinha, S. Vartak, A. Bhartiya, and S. Kumar, "LC determination of glimepiride and its related impurities," *J. Pharm. Biomed. Anal.*, vol. 39, no. 5, pp. 928–943, 2005.

[35]P. Sahoo, R. Sharma, and S. Chaturvedi, "Simultaneous estimation of metformin hydrochloride and pioglitazone hydrochloride by RPHPLC method from combined tablet dosage form," *Indian J. Pharm. Sci.*, vol. 70, no. 3, pp. 383–386, 2008.

[36]J. Yao, Y. Q. Shi, Z. R. Li, and S. H. Jin, "Development of a RP-HPLC method for screening potentially counterfeit anti-diabetic drugs," *J. Chromatogr. B Anal. Technol. Biomed. Life Sci.*, vol. 853, no. 1–2, pp. 254–259, 2007.

[37]J. Shaodong, W. J. Lee, J. W. Ee, J. H. Park, S. W. Kwon, and J. Lee, "Comparison of ultraviolet detection, evaporative light scattering detection and charged aerosol detection methods for liquid-chromatographic determination

of anti-diabetic drugs," *J. Pharm. Biomed. Anal.*, vol. 51, no. 4, pp. 973–978, 2010.

[38] S. Samala, S. R. Tatipamula, and C. Veeresham, "Determination of Glimepiride in Rat Serum by Rp-Hplc Method," *Am. J. Anal. Chem.*, vol. 02, no. 02, pp. 152–157, 2011.

[39] S. R. Polagani, N. R. Pilli, R. Gajula, and V. Gandu, "Simultaneous determination of atorvastatin, metformin and glimepiride in human plasma by LC-MS/MS and its application to a human pharmacokinetic study," *J. Pharm. Anal.*, vol. 3, no. 1, pp. 9–19, 2013.

[40] A. Kumar, A. K. Sharma, and R. Dutt, "Reverse-phase high-performance liquid chromatography method development and validation for estimation of glimepiride in bulk and tablet dosage form," *Int. J. Pharm. Qual. Assur.*, vol. 11, no. 2, pp. 299–305, 2020.

[41] A. B. Mohd, K. Sanka, R. Gullapelly, P. V. Diwan, and N. Shastri, "Development and validation of RP-HPLC method for glimepiride and its application for a novel self-nanoemulsifying powder (SNEP) formulation analysis and dissolution study," *J. Anal. Sci. Technol.*, vol. 5, no. 1, pp. 1–8, 2014.

[42] I. M. de O. Viana, P. de P. R. Lima, C. D. V. Soares, and C. Fernandes, "Simultaneous determination of oral antidiabetic drugs in human plasma using microextraction by packed sorbent and high-performance liquid chromatography," *J. Pharm. Biomed. Anal.*, vol. 96, pp. 241–248, 2014.

[43] S. Zhou, P. Zuo, Y. Zuo, and Y. Deng, "A rapid hydrophilic interaction liquid chromatographic determination of glimepiride in pharmaceutical formulations," *Saudi Pharm. J.*, vol. 25, no. 6, pp. 852–856, 2017.