1. Introduction

Statins are used in medical practice for the prevention and treatment of hypercholesterolemia. Rosuvastatin is one of the most powerful statins available in the pharmaceutical market. Rosuvastatin was first introduced to the pharmaceutical market about 10 years ago. During that time, its effectiveness and safety have been carefully evaluated in a wide variety of patient cohorts in many clinical studies [1]. Rosuvastatin (Fig. 1), bis[(3R,5S,6E)-7-[4-(4-fluorophenyl)-2-(N-methylmethanesulfonamido)-6-(propan-2-yl)pyrimidin-5-yl]-3,5-dihydroxyhept-6-enoate] – sparingly soluble in water (17.96 mg/mL), Log $P = 0.13$ [2].

Differently from other statins, adding a stable polar methane sulfonamide group in the structure of rosuvastatin confers relatively low lipophilicity [3, 4]. The European Pharmacopoeia (Ph. Eur.) has a monograph on rosuvastatin calcium and tablets [5]. Ph. Eur. regulates the quantitative determination of rosuvastatin in tablets by HPLC. Brazilian scientists conducted a thorough review of literature sources on the development of analytical methods for the analysis of rosuvastatin in dosage forms and biological fluids [6]. Many spectrophotometric [7–23] and chromatographic methods [24–41] are described in the scientific literature. Nowadays, chromatographic techniques are undoubtedly the most modern in terms of specificity, correctness and precision. However, there are laboratories that do not have expensive equipment, and for them, spectrophotometric methods of analysis are more accessible. Spectrophotometric methods are often used as alternatives in implementing quality control of medicines. The scientific literature describes a number of spectrophotometric methods for determining rosuvastatin in dosage forms by its own absorption [24–42]. Considering the advantages of using
sulfophthalein dyes in pharmaceutical analysis, the spectrophotometric method for determining rosuvastatin by reaction with bromocresol green, developed by Syrian scientists, deserves attention [13]. However, the proposed technique involves the use of chloroform as a solvent, which does not confirm the principles of «green» chemistry. Taking into account the facts described above, we became interested in developing spectrophotometric methods for determining rosuvastatin by reaction with sulfophthalein dyes in compliance with the principles of «green» chemistry. The chemistry of sulfophthalein dyes and the development of spectrophotometric methods for determining APIs in dosage forms based on interaction with sulfophthalein dyes is interesting and not easy, as it requires the use of certain approaches to the research methodology. At the preliminary research stage, we tested many sulfophthalein dyes and the results obtained when using bromophenol blue (BPB) were interesting. Therefore, the aim of our work was to develop a spectrophotometric method for the determination of rosuvastatin in tablets based on the reaction with BPB in compliance with the principles of «green» chemistry.

2. Planning of the research

Methodology of research of development and validation of the spectrophotometric methods for the determination of rosuvastatin in tablets in compliance with the principles of «green» chemistry includes:

1. Analysis of the monograph of Ph. Eur. 11 edition and scientific articles.
2. Study of reaction conditions between rosuvastatin calcium and BPB (choice of sulfophthalein dye, solvent, optimal volume and concentration of reagent, optimal wavelength, stability, detection of stoichiometric coefficients).
3. Validation of the spectrophotometric method for determination of rosuvastatin in tablets.
4. Evaluation of the greenness profile assessment of the proposed method.

3. Materials and methods

All research was conducted in the Department of Pharmaceutical Chemistry, I. Horbachevsky Ternopil National Medical University, Maidan Voli 1, 46001 Ternopil, Ukraine (2022 year).

Objects of study, solvents and equipment.

Analytical equipment: two-beam UV-visible spectrophotometer Shimadzu model -UV 1800 (Japan), software UV-Probe 2.62, electronic laboratory balance RAD WAG AS 200/C (Poland).

The following APIs, dosage forms, reagents and solvents were used in work: pharmacopeial standard sample (CRS) of rosuvastatin calcium (Sigma-Aldrich, ≥98 %, HPLC), BPB (Sigma-Aldrich, ≥98 %, HPLC), “Rosuvastatin” tablets 10 mg, 15 mg, 20 mg, methanol (Honeywell, ≥99.9 %, GC), ethanol (Honeywell, ≥99.9 %, GC), chloroform (Honeywell, ≥99.9 %, GC), acetonitrile (Honeywell, ≥99.9 %, GC), and ethyl acetate (Honeywell, ≥99.7 %, GC).

Proposed procedure for the determination of rosuvastatin calcium with BPB.

20.00 mg of CRS rosuvastatin calcium was transferred into a 50.00 mL volumetric flask with 35 mL acetonitrile. The mixture was shaken and diluted to volume with acetonitrile. Aliquot 0.50 mL was added to 0.5 mL of 4.0×10⁻⁴ M BPB in acetonitrile. The volume of 10.00 mL was made up to the mark by adding acetonitrile. The absorbance of the resulting solution was measured against the background of the compensating solution (a solution containing all components except the analyte) at a wavelength of 595 nm.

Procedure for tablets for the determination of rosuvastatin calcium with BPB.

Twenty tablets were accurately weighed and powdered. A quantity of powder containing 20.00 mg of rosuvastatin calcium was transferred into a 50.00 mL volumetric flask with 35 mL acetonitrile. The mixture was shaken for 15 minutes, diluted to volume with acetonitrile, and then filtered. Aliquot 0.50 mL was added to 0.5 mL of 4.0×10⁻⁴ M BPB in acetonitrile. The volume of 10.00 mL was made up to the mark by adding acetonitrile. The absorbance of the resulting solution was measured against the background of the compensating solution (a solution containing all components except the analyte) at a wavelength of 595 nm.

4. Research results

4. 1. Selection of reaction conditions

As mentioned above, the scientific literature describes the development of one spectrophotometric method for determining rosuvastatin in tablets by reaction with bromocresol green through ion-pair complex formation at the wavelength of the absorbance maximum at 416 nm in a chloroform medium [13]. However, using chloroform as a solvent makes it impossible to use the proposed analytical method as eco-friendly. Taking into account the described fact, we set ourselves the task of developing an environmentally safe spectrophotometric method for the determination of rosuvastatin.
in tablets by reaction with sulfophthalein dyes. We tested such sulfophthalein dyes as BPB, bromocresol green, bromocresol purple, and others. Each of the above sulfophthalein dyes gave positive results in the experiment. For further work, we chose BPB as a promising reagent for developing a spectrophotometric method for determining rosuvastatin in tablets. In the acetonitrile solution, the band of the monoanionic form of BPB predominates. In the presence of rosuvastatin, the acid-base balance of the dye shifts towards the doubly deionized form since rosuvastatin forms a more stable ionic associates with this form of the dye (Fig. 2). Rosuvastatin forms complexes with BPB with an absorbance maximum at a wavelength of 595 nm (Fig. 2). In the process of experimental studies, it was established that the optimal concentration of BPB is $4.00 \times 10^{-4}$ M.

We selected optimal conditions for the reaction in order to form a coloured product of the reaction with maximum stability and sensitivity. The maximum absorbance was observed in the acetonitrile solution with BPB, which we chose for further research (Fig. 3).

![Fig. 2. The spectra of absorbance of the reaction product of rosuvastatin calcium with BPB in acetonitrile medium](image)

An important aspect in the development of the spectrophotometric method is the study of stability since the research data will also affect the robustness of the analytical method. We have studied the stability of solutions over time. It was established that the obtained solutions were stable for 45 minutes (Fig. 4).

![Fig. 4. Graph of the dependence of the absorbance of the reaction product of rosuvastatin calcium with BPB in acetonitrile solution depending on time](image)

The stoichiometric coefficients of the reacting components between rosuvastatin calcium and BPB were determined by continuous changes (Job’s method) and the saturation method (the method of molar ratios). Fig. 5 illustrates the study of the stoichiometric coefficients of the reacting components by the method of continuous changes. At the same time, Fig. 6 shows the study results of the stoichiometric coefficients of the reacting components by the method of molar ratios. As seen from Fig. 5, 6, the stoichiometric coefficients of the reacting components between rosuvastatin calcium and BPB correspond 1: 1.

As shown in Fig. 7, the optimal volume of $4.0 \times 10^{-4}$ M solution BPB is 0.5 mL.

The sensitivity of the reaction between rosuvastatin calcium and BPB was calculated. The molar absorption ($\varepsilon$) was $1.37 \times 10^4$, the specific absorption ($a$) was 0.14, and the Sendel coefficient ($W_s$) was 0.073. The sensitivity parameters indicate a high sensitivity of the reaction between rosuvastatin calcium and BPB.

![Fig. 5. Graph of the dependence of the amount of absorbance on the composition of the isomolar solution: $V_1 = 4.0 \times 10^{-4}$ M rosuvastatin calcium solution; $V_2 = 4.0 \times 10^{-4}$ M solution BPB at 595 nm](image)
4.2. Determination of validation characteristics

The proposed spectrophotometric method for the determination of rosuvastatin calcium in tablets by reaction with BPB has been validated in accordance with the requirements of SPhU for the following indicators: specificity, linearity, range of application, accuracy, precision and robustness.

4.2.1. Specificity

The results of studying the specificity of the spectrophotometric method are presented in Table 1. The absorbance of auxiliary substances is insignificant (the found value of δ noise is 0.37 %) and does not exceed the acceptance criterion (Table 1).

| Indicator          | Value       | Criteria | Conclusion |
|--------------------|-------------|----------|------------|
| b=S(δ)             | 0.0178±(0.0091) | –        | –          |
| a=S(δ)             | -0.0542±(0.0042) | >2.6     | Corresponds|
| R²                 | 0.9979      | >0.9961  | Corresponds|
| LOD (µmol/L)       | 0.77        | –        | –          |
| LOQ (µmol/L)       | 2.36        | –        | –          |
| Beer’s law limits (µmol/L) | 7.99–23.97 | –        | –          |

Analyzing Fig. 8 and Table 2, it can be concluded that a linear dependence is observed in the range of concentrations 7.99–23.97 µmol/L. The LOD and LOQ values were calculated to be 0.77 µmol/L and 2.36 µmol/L.

4.2.3. Accuracy and precision

The accuracy and precision study of the spectrophotometric method for the determination of rosuvastatin in tablets by reaction with BPB was carried out on model solutions. The results of the accuracy and precision study are given in Table 3.

The systematic error of the method (0.16 %) was statistically and practically insignificant, i.e. spectrophotometric method was characterized by sufficient accuracy in the whole range of analyzed concentrations.

The study of intra-laboratory precision was carried out on six samples of the same series of tablets, by different analysts, on different days, using flasks of different volumes, by estimating the value of the relative confidence interval, which should be less than the maximum permissible uncertainty of the analysis results: ∆z ≤1.6 (at B=5 %) (Table 4).

The intra-laboratory precision of the analysis results is confirmed by the fact that the value of the relative confidence interval for six parallel determinations of one series of drugs meets the acceptance criterion (≤1.6 %) (Table 4).
4.2.4. Robustness

The study of robustness was carried out during the development of the analytical method. The stability of solutions over time and the amount of added reagent (BPB) was established.

A study of the robustness of the analytical method showed that the analyzed solutions were stable for 45 min (Fig. 4), and fluctuations in the amount of added BPB within ±10% did not significantly affect the absorbance (Table 5).

Table 5

| Amount of BPB, mL | % BPB | A |
|------------------|------|---|
| 0.45             | 90   | 0.261 |
| 0.50             | 100  | 0.273 |
| 0.55             | 110  | 0.278 |

4.3. Application to tablet analysis

After performing the validation procedure of the analytical method, which was carried out on model solutions, we applied the analytical method for the determination of rosuvastatin calcium in tablets. The results of the quantitative determination of rosuvastatin calcium in tablets are presented in Table 6.

Table 6

| Drug               | Found, g | Metrological characteristics |
|--------------------|----------|-----------------------------|
| Tablets Rosuvastatin 20 mg | 0.0204 | $\bar{m} = 0.0208 \text{ g}$ |
| Tablets Rosuvastatin 15 mg | 0.0150 | $\Delta x = 5.75 \times 10^{-4}$ |
| Tablets Rosuvastatin 10 mg | 0.0099 | RDS=0.36 |

The average value, $Z$, % 100.16

Standard deviation, $S_z$, % 0.39

Relative confidence interval $\Delta Z = (95 \%, 8) S_z = 2.3060 \% 0.90$

The critical value for the convergence of results $\Delta x = 0.16$

Systematic error $\delta = -|Z| 100\% 0.16$

The criterion of uncertainty of systematic error $\delta \leq 0.51$

General conclusion Correct

Table 3

The results of intra-laboratory precision study

| No. solution | Value $Z$, % |
|--------------|--------------|
| 1            | 100.05       |
| 2            | 100.01       |
| 3            | 99.95        |
| 4            | 99.98        |
| 5            | 100.12       |
| 6            | 99.92        |
| Average $Z$, % | 100.01       |

RSD, % 0.07

Relative standard deviation, RSDZ (%) 0.10

Relative confidence interval, $\Delta Z \leq 1.6$

The critical value of the convergence of results, $\Delta x \leq 1.6$

Table 4

The results of quantitative determination of rosuvastatin calcium in tablets

| Drug               | Found, g | Metrological characteristics |
|--------------------|----------|-----------------------------|
| Tablets Rosuvastatin 20 mg | 0.0204 | $\bar{m} = 0.0208 \text{ g}$ |
| Tablets Rosuvastatin 15 mg | 0.0150 | $\Delta x = 5.75 \times 10^{-4}$ |
| Tablets Rosuvastatin 10 mg | 0.0099 | RDS=0.36 |

The average value, $Z$, % 100.16

Standard deviation, $S_z$, % 0.39

Relative confidence interval $\Delta Z = (95 \%, 8) S_z = 2.3060 \% 0.90$

The critical value for the convergence of results $\Delta x = 0.16$

Systematic error $\delta = -|Z| 100\% 0.16$

The criterion of uncertainty of systematic error $\delta \leq 0.51$

General conclusion Correct
4.4. Assessment of the impact of the analytical method on the environment

As mentioned above, one of the main tasks was to develop an environmentally safe spectrophotometric method for the determination of rosuvastatin in tablets by reaction with BPB. Assessment of the «greenness» of the spectrophotometric method was performed using AGREE tool (Analytical GREEnness), GAPI (Green Analytical Procedure Index) and analytical eco-scale. A pictogram of the analytical method using AGREE tool is illustrated in Fig. 9. Pictogram of the analytical method using the GAPI tool is illustrated in Fig. 10. The score of the analytical method using AGREE tool was 0.77 (Fig. 9). The score of the analytical eco-scale was 90 (Table 7).

Table 7

| Parameters          | Penalty points |
|---------------------|----------------|
| Reagents            | –              |
| BPB                 | 1              |
| Acetonitrile        | 3              |
| Energy              | 1              |
| Waste               | 5              |
| Total number of penalty points | 10       |
| Ball of analytical eco-scale | 90        |
| Conclusion          | Excellent «green» analysis |

Fig. 9. Pictogram of an analytical method using AGREE tool

Fig. 10. Pictogram of an analytical method using GAPI tool

As can be seen from Table 7 and Fig. 9, 10, the spectrophotometric method for the determination of rosuvastatin in tablets based on the reaction with BPB was eco-friendly.

5. Discussion of research results

The scientific literature describes the development of one spectrophotometric method for the determination of rosuvastatin in tablets by reaction with bromocresol green [13]. Scientists have proposed a scheme for the interaction of rosuvastatin with bromocresol green with the ion-pair complex formation, and the optimal conditions for the reaction have been investigated. Comparative optimum conditions for spectrophotometric determination are presented in Table 8.

Table 8

| Parameters                  | [23] Developed method |
|-----------------------------|-----------------------|
| Reagent                     | bromocresol green     | bromophenol blue       |
| Solvent                     | chloroform            | acetonitrile           |
| Wavelength, nm              | 416                   | 595                    |
| The molar absorptivity of complex (ε) | 1.92×10⁴  | 1.37×10⁹ |
| Working concentration of reagent, mol/L | 1×10⁻⁴  | 4×10⁻⁴ |

As we can see from Table 8, our proposed method does not require the use of a toxic solvent and, accordingly, is developed in accordance with the principles of «green chemistry», which is an advantage of the method. The molar absorptivity is high (1.37×10⁹), which indicates the sensitivity of the reaction. The stoichiometric ratios of the reactive components as 1:1 were obtained by the methods of continuous changes and the saturation method. The developed analytical method was validated in accordance with the requirements of the SPhU. The linearity regression equation was y=0.0178x−0.0542, and the obtained correlation coefficient was R²=0.9979 (Table 2, Fig. 8). The linear relationship was found between absorbance at λmax and concentration of rosuvastatin in the range 7.99-23.97 µmol/L. The LOD and LOQ values were calculated to be 0.77 µmol/L and 2.36 µmol/L. The results of studying the accuracy and precision of the analytical method showed compliance with the acceptance criteria (Tables 3, 4). The results of studying the robustness of the analytical method indicate that the change in the amount of added reagent (BPB) does not affect the results of the analysis (Table 5), and the solutions are stable for 45 minutes (Fig. 4). We conducted the study of the «greenness» of the developed analytical method. Taking into account the obtained score of the eco-scale (Table 7) and the AGREE and GAPI tools (Fig. 9, 10), the results show that the spectrophotometric method of the determination of rosuvastatin in tablets by reaction with BPB is «green» and eco-friendly.

**Study limitations.** The developed spectrophotometric method can not be used to determine rosuvastatin in the presence of other statins.

**Prospects for further research.** This article describes the main stages of the spectrophotometric method development of rosuvastatin in tablets based on the reaction with BPB. The next stage of research is planned to develop and validate the spectrophotometric method for the determination of rosuvastatin in tablets based on the reaction with other sulfophthalein dyes.

6. Conclusion

An eco-friendly spectrophotometric method has been developed for the quantitative determination of rosuvastatin in tablets based on the reaction with BPB. The ap-
propriate sulfophthalein dye (BPB) and its concentration (4.00×10−4), the optimal volume of reagent (0.5 mL), the optimal eco-friendly solvent (acetonitrile), the appropriate wavelength (595 nm) were chosen, and the sensitivity of the reaction were calculated. The stoichiometric ratios of the reactive components as 1:1 were obtained by the methods of continuous changes and the saturation method. Validation of the analytical method was carried out and its possibility for use in the pharmaceutical analysis was shown.

Conflict of interest
The authors declare that they have no conflict of interest in relation to this research, whether financial, personal, authorship or otherwise, that could affect the research and its results presented in this paper.

References
1. Barna, O. M. (2013). Efficient and effective cardiovascular prevention: the role of rosuvastatin. Ukrainskiy medychnyi chasopys, 5 (97), 93–98.
2. Vapor Pressure. Rosuvastatin. Available at: http://pubchem.ncbi.nlm.nih.gov/compound/Rosuvastatin#section–Vapor-Pressure
3. Buckett, L., Ballard, P., Davidson, R., Dunkley, C., Martin, L., Stafford, J., McTaggart, F. (2000). Selectivity of ZD4522 for inhibition of cholesterol synthesis in hepatic versus non-hepatic cells. Atherosclerosis, 151 (1), 41. doi: https://doi.org/10.1016/s0021-9150(00)80185-9
4. Smith, G., Davidson, R., Bloor, S., Burns, K., Calnan, C., McAulay, P., Torr, N., Ward, W., McTaggart, F. (2000). Pharmacological properties of ZD4522 – A new HMG-CoA reductase inhibitor. Atherosclerosis, 151 (1), 39. doi: https://doi.org/10.1016/s0021-9150(00)80176-8
5. European Pharmacopoeia (2022). Available at: https://www.epdqm.eu/en/web/edqm/european-pharmacopoeia-ph-eur-11th-edition
6. Ângelo, M. L., Moreira, F. de L., Morais Ruela, A. L., Santos, A. L. A., Salgado, H. R. N., de Araújo, M. B. (2018). Analytical Methods for the Determination of Rosuvastatin in Pharmaceutical Formulations and Biological Fluids: A Critical Review. Critical Reviews in Analytical Chemistry, 48 (4), 317–329. doi: https://doi.org/10.1080/10408347.2018.1439364
7. Uyar, B., Celebier, M., Altinöz, S. (2007). Spectrophotometric determination of rosvustatin calcium in tablets. Die Pharmazie-An International Journal of Pharmaceutical Sciences, 62 (6), 411–413.
8. Gupta, A., Mishra, P., Shah, K. (2009). Simple UV Spectrophotometric Determination of Rosuvastatin Calcium in Pure Form and in Pharmaceutical Formulations. E-Journal of Chemistry, 6 (1), 89–92. doi: https://doi.org/10.1155/2009/956712
9. Krishna, M. V., Sankar, D. G. (2007). Extractive Spectrophotometric Methods for the Determination of Rosuvastatin Calcium in Pure Form and in Pharmaceutical Formulations by Using Safranin O and Methylene blue. E-Journal of Chemistry, 4 (1), 46–49. doi: https://doi.org/10.1155/2007/454853
10. Ramadan, A. A., Mandil, H. A. S. N. A., Alshelhawi, N. O. O. R. (2014). Spectrophotometric determination of rosuvastatin calcium in pure form and pharmaceutical formulations by the oxidation using iodine and formation triiodide complex in acetonitrile. International Journal of Pharmaceutical and Pharmaceutical Sciences, 6 (5), 579–585.
11. Lima, M. F., Cassella, R. J., Pacheco, W. F. (2017). Spectrophotometric determination of rosuvastatin in pharmaceutical formulations using quinalizarin. Brazilian Journal of Pharmaceutical Sciences, 53 (3). doi: https://doi.org/10.1590/s2175-97902017000300075
12. Braga, V. S. M., Mancilha, T. P., Cassella, R. J., Pacheco, W. F. (2012). Determination of Rosuvastatin in Urine by Spectrofluorimetry After Liquid–Liquid Extraction and Derivatization in Acidic Medium. Journal of Fluorescence, 23 (1), 49–55. doi: https://doi.org/10.1007/s10895-011-1154-4
13. Ramadan, A. A., Mandil, H. A. S. N. A., Alsayed-Ali, R. A. F. I. F. (2015). Spectrophotometric determination of rosuvastatin in pure form and pharmaceutical formulations through ion-pair complex formation using bromocresol green. International Journal of Pharmacy and Pharmaceutical Sciences, 7 (11), 191–198.
14. Prajapati, P. B., Bodiwala, K. B., Marolia, B. P., Rathod, I. S., Shah, S. A. (2010). Development and validation of extractive spectrophotometric method for determination of rosvustatin calcium in pharmaceutical dosage forms. Journal of Pharmacy Research, 3 (8), 2036–2038.
15. Ângelo, M. L. (2016). Análise químico-farmacêutica de rosuvastatina cálcica comprimido e cápsula. Brazil.
16. Sevda, R. R., Ravetkar, A. S., Shirote, P. J. (2011). UV Spectrophotometric estimation of rosuvastatin calcium and fenofibrate in bulk drug and dosage form using simultaneous equation method. International Journal of ChemTech Research, 3 (2), 629–635.
17. El-Bagary, R. I., ElKady, E. F., Kadry, A. M. (2012). Spectrofluorometric Determination of Certain Anti-hyperlipidemic Agents in Bulk and Pharmaceutical Preparations. Spectroscopy: An International Journal, 27, 83–92. doi: https://doi.org/10.1155/2012/913913
18. Patel, B., Jadav, A., Solanki, H., Parmar, S., Parmar, V., Captain, A. (2013). Development and validation of derivative spectroscopic method for the simultaneous estimation of rosuvastatin calcium and fenofibrate in tablet. International Journal of Pharma Research & Review, 2 (7), 1–6.
19. Ambole, S. R., Shirote, P. J., Kondawar, M. S. (2012). Simultaneous Estimation for Rosuvastatin calcium and Aspirin from Capsule Dosage Forms by First Order. Derivative Spectroscopic Method. International Journal of ChemTech Research, 4 (3), 966–970.
20. Karunakaran, A., Subhash, V., Chinthala, R., Muthuvijayan, J. (1970). Simultaneous Estimation of Rosuvastatin Calcium and Fenofibrate in Bulk and in Tablet Dosage Form by UV-Spectrophotometry and RP-HPLC. Stamford Journal of Pharmaceutical Sciences, 4 (1), 58–63. doi: https://doi.org/10.3329/sjps.v4i1.8868

21. Sharma, S., Bhandari, P. (2005). Simultaneous Estimation of Rosuvastatin Calcium and Fenofibrate in Bulk and in Tablet Dosage Form by UV-Spectrophotometry and RP-HPLC. Journal of Pharmacy Research, 5, 2311–2314.

22. Afroz, A., Haque, T., Talukder, M. U., Islam, S. M. (2011). Spectrophotometric estimation of rosuvastatin calcium and glimepiride in tablet dosage form. Asian Journal of Pharmaceutical analysis, 1 (4), 74–78.

23. Parmar, V., Solanki, H., Prajapati, L. (2013). Derivative spectrophotometric determination of rosuvastatin calcium and fenofibrate in tablet dosage form. Inveti Rapid: Pharm Analysis & Quality Assurance, 2, 1–5.

24. Dudhipala, N., Veerabrahma, K. (2017). Improved anti-hyperlipidemic activity of Rosuvastatin Calcium via lipid nanoparticles: Pharmacokinetic and pharmacodynamic evaluation. European Journal of Pharmaceutics and Biopharmaceutics, 110, 47–57. doi: https://doi.org/10.1016/j.ejpb.2016.10.022

25. Nazir, S., Iqbal, Z., Nasir, F. (2015). Impact of Menopause on Pharmacokinetics of Rosuvastatin Compared with Premenopausal Women. European Journal of Drug Metabolism and Pharmacokinetics, 41 (5), 505–509. doi: https://doi.org/10.1007/s13318-015-0285-2

26. Beluradi, M. I., Prakash, K. V., Mohan, G. K. (2013). RP-HPLC method for simultaneous estimation of Rosuvastatin and Ezetimibe from their combination tablet dosage form. International Journal of Chemical and Analytical Science, 4 (4), 205–209. doi: https://doi.org/10.1016/j.ijcas.2013.04.006

27. Balakumar, K., Raghavan, C. V., selvan, N. T., prasad, R. H., Abdu, S. (2013). Self nanoemulsifying drug delivery system (SNEDDS) of Rosuvastatin: Design, formulation, bioavailability and pharmacokinetic evaluation. Colloids and Surfaces B: Biointerfaces, 112, 337–343. doi: https://doi.org/10.1016/j.colsurfb.2013.08.025

28. Kumar, T. R., Shitut, N. R., Kumar, P. K., Vinu, M. C. A., Kumar, V. V. P., Mullangi, R., Srinivas, N. R. (2006). Determination of rosuvastatin in rat plasma by HPLC: validation and its application to pharmacokinetic studies. Biomedical Chromatography, 20(9), 881–887. doi: https://doi.org/10.1002/bmc.611

29. Caglar, S., Toker, S. (2012). Determination of Rosuvastatin at Picogram Level in Serum by Fluorimetric Derivatization with 9-Anthryldiazomethane using HPLC. Journal of Chromatographic Science, 51 (1), 53–58. doi: https://doi.org/10.1093/chromsci/bms105

30. Eswarudu, M. M., Mounica, P., Venkatesh, D., Nagalakshmi, B. (2012). Method Development and Validation for Simultaneous Estimation of Rosuvastatin Calcium and Ezetimibe in Pharmaceutical Dosage Form by RP-HPLC. International Research Journal of Pharmaceutical and Applied Sciences, 2, 24–36.

31. Trivedi, H. K., Patel, M. C. (2012). Development and Validation of a Stability-Indicating RP-UPLC Method for Determination of Rosuvastatin and Related Substances in Pharmaceutical Dosage Form. Scientia Pharmaceutica, 80 (2), 393–406. doi: https://doi.org/10.3797/scipharm.1201-09

32. Rao, A. L., Suneetha, D. (2010). Development and validation of RP-HPLC method for the estimation of rosuvastatin in bulk and pharmaceutical dosage form. International Journal of Chemical Science, 8 (2), 1308–1314.

33. Haq, N., Shakeel, F., Alanazi, F., Alshora, D. H., Ibrahim, M. A. (2018). Development and validation of a green RP-HPLC method for the analysis of rosuvastatin: a step towards making liquid chromatography environmentally benign. Green Processing and Synthesis, 7 (2), 160–169. doi: https://doi.org/10.1515/gps-2017-0023

34. Mostafa, N. M., Badaweey, A. M., Lamie, N. T., Abd El-Aleem, A. E. A. B. (2014). Selective chromatographic methods for the determination of Rosuvastatin calcium in the presence of its acid degradation products. Journal of Liquid Chromatography & Related Technologies, 37 (15), 2182–2196. doi: https://doi.org/10.1080/10826076.2013.828305

35. Kaila, H., Ambasana, M., Thakkar, R., Saravaia, H., Shah, A. (2010). A new improved RP-HPLC method for assay of rosuvastatin calcium in tablets. Indian Journal of Pharmaceutical Sciences, 72 (5), 592–598. doi: https://doi.org/10.4103/0250-474x.78526

36. Hassouna, M. K. M., Abdel-Mageed, A. I., Salem, H. O. (2017). Indirect Oxygen-Flash Atomic Absorption Spectrometric Determination of Rosuvastatin Calcium. Biomedical Journal of Scientific & Technical Research, 1, 1–6. doi: https://doi.org/10.26717/bjstr.2017.01.000164

37. Sree Janardhanan, V., Manavalan, R., Valliappan, K. (2016). Chromometric technique for the optimization of chromatographic system: Simultaneous HPLC determination of Rosuvastatin, Telmisartan, Ezetimibe and Atorvastatin used in combined cardiovascular therapy. Arabian Journal of Chemistry, 9, S1378–S1387. doi: https://doi.org/10.1016/j.arabjc.2012.03.001

38. Kishore, C. R. P., Mohan, G. V. K. (2017). Structural identification and estimation of Rosuvastatin calcium related impurities in Rosuvastatin calcium tablet dosage forms. Analytical Chemistry Research, 12, 17–27. doi: https://doi.org/10.1016/j.arcnr.2016.11.002

39. Shah, Y., Iqbal, Z., Ahmad, L., Khan, A., Khan, M. I., Nazir, S., Nasir, F. (2011). Simultaneous determination of rosuvastatin and atorvastatin in human serum using RP-HPLC/UV detection: Method development, validation and optimization of various experimental parameters. Journal of Chromatography B, 879 (9-10), 557–563. doi: https://doi.org/10.1016/j.jchromb.2011.01.004

40. Vittal, S., Shitut, N. R., Kumar, T. R., Vinu, M. C. A., Mullangi, R., Srinivas, N. R. (2006). Simultaneous quantification of rosuvastatin and gemfibrozil in human plasma by high-performance liquid chromatography and its application to a pharmacokinetic study. Biomedical Chromatography, 20 (11), 1252–1259. doi: https://doi.org/10.1002/bmc.692

41. Gomes, F. P., Garcia, P. L., Porto Alves, J. M., Singh, A. K., Kedor-Hackmann, E. R. M., Miritello Santoro, M. I. R. (2009). Development and Validation of Stability-Indicating HPLC Methods for Quantitative Determination of Pravastatin, Fluvastatin, Atorvastatin, and Rosuvastatin in Pharmaceuticals. Analytical Letters, 42 (12), 1784–1804. doi: https://doi.org/10.1080/00032710903060669

42. Derzhavna farmakopeia Ukrainy. Vol. 1 (2015). Kharkiv: DP «Ukrainskyi naukovyi tsentr yakosti likarskykh zasobiv», 1128.
Liudmyla Halka, Postgraduate Student, Department of Pharmaceutical Chemistry, I. Horbachevsky Ternopil National Medical University, Voli sq., 1, Ternopil, Ukraine, 46001

Tetyana Kucher, PhD, Associate Professor, Department of Pharmaceutical Chemistry, I. Horbachevsky Ternopil National Medical University, Voli sq., 1, Ternopil, Ukraine, 46001

Liubomyr Kryskiw, PhD, Associate Professor, Department of Pharmaceutical Chemistry, I. Horbachevsky Ternopil National Medical University, Voli sq., 1, Ternopil, Ukraine, 46001

Marjan Piponsk, PhD, Head of Department, Instrumental Analysis, Quality Control Department, Replek Farm Ltd. Company for pharmaceutical-chemical products, Kozle str., 188, Skopje, Republic of Macedonia, 1000

Iryna Furdela, Department of Pharmaceutical Chemistry, I. Horbachevsky Ternopil National Medical University, Voli sq., 1, Ternopil, Ukraine, 46001

Tetyana Uglyar, PhD, Associate Professor, Department of Oncology, Radiodiagnosis, Radiotherapy and Radiation Medicin, I. Horbachevsky Ternopil National Medical University, Voli sq., 1, Ternopil, Ukraine, 46001

Olha Poliak, PhD, Associate Professor, Department of Pharmaceutical Chemistry, I. Horbachevsky Ternopil National Medical University, Voli sq., 1, Ternopil, Ukraine, 46001

Liliya Logoyda*, Doctor of Pharmaceutical Sciences, Professor, Head of Department, Department of Pharmaceutical Chemistry, I. Horbachevsky Ternopil National Medical University, Voli sq., 1, Ternopil, Ukraine, 46001

*Corresponding author: Liliya Logoyda, e-mail: logojda@tdmu.edu.ua