Veterinarski Glasnik 2017, 71 (2), 87-97
UDC: 615.33.074
https://doi.org/10.2298/VETGL1702087S

Mini Review

OVERVIEW OF THE ANALYTICAL METHODS FOR VANCOMYCIN AND/OR TEICOPLANIN DETERMINATION IN BIOLOGICAL MATRICES

STAJIĆ Ana[1], JANČIĆ-STOJANOVIĆ Biljana[1*]

[1]University of Belgrade, Faculty of Pharmacy, Department of Drug Analysis, Belgrade, Serbia

Received 06 August 2017; Accepted 22 October 2017
Published on-line: 30 November 2017

Abstract

Background. Teicoplanin and vancomycin are glycopeptide antibiotics currently in use for treatment of multidrug-resistant bacterial infections.

Scope and Approach. Severe undesirable effects, such as ototoxicity, nephrotoxicity and neutropenia have been reported for vancomycin and teicoplanin, which necessitates monitoring the concentration of these two drugs in different biological samples. In order to obtain precise and accurate results, sensitive, reliable and fast methods are necessary. The main aim of this mini review is to give a clear and concise overview of the recently developed, validated, novel and improved methods for glycopeptide antibiotic analyses in various biological matrices. Also, the variability of the matrices requires optimal and effective sample preparation procedures to be developed, and so these are discussed.

Key Findings and Conclusions. Different liquid chromatography-tandem mass spectrometry (LC-MS/MS) methods have been described for quantitative determination of glycopeptide antibiotics in various biological matrices. It was shown that protein precipitation was a convenient method for sample preparation despite the high number of novel sample preparation methods.

Key Words: Vancomycin, teicoplanin, biological samples, determination, LC-MS/MS

INTRODUCTION

Multidrug-resistant (MDR) bacterial infections have become one of the most serious problems worldwide (Jyoti et.al, 2014). Glycopeptide antibiotics including vancomycin

*Corresponding author – e-mail: jancic.stojanovic@pharmacy.bg.ac.rs

and teicoplanin are the first-line antibiotics for treatment of MDR infections (Jyoti et.al, 2014, Poonam Sood et al., 2010). These drugs are not effective against gram negative infections, and are currently in use for the treatment of gram positive bacterial infections, especially those caused by methicillin-resistant S. aureus (MRSA) (Jyoti et.al, 2014). Their main mechanism of action is inhibition of the growth of susceptible organisms by interfering with cell-wall synthesis. Peptidoglycan synthesis is blocked by specific binding to D-alanyl-D-alanine residues (Kang & Park, 2015). Severe undesirable effects, such as ototoxicity, nephrotoxicity and neutropenia have been reported for vancomycin (Donald et al., 2006). Teicoplanin has a less toxic potential than vancomycin, but ototoxicity and nephrotoxicity have also been registered (Svetitsky et al., 2009). On the other hand, insufficient doses of these two drugs could lead to antibiotic resistance and disease progression. In order to ensure sufficient levels for therapeutic efficacy and avoid toxic levels of these two drugs, monitoring the drug concentrations is needed and highly recommended.

According to the literature, different analytical methods have been reported for determination of vancomycin and/or teicoplanin in various matrices. The main aim of this review is to provide a detailed overview of published methods for determining the concentration of vancomycin and/or teicoplanin in different types of samples in recent years, focusing on 2014-2017. Reviews were published in 2007, and 2015 dealing with the methods for vancomycin determination only and sample preparation (Vila et al., 2007; Javorska et. al., 2016). Although a recently published review covered the methods published by 2015 for vancomycin determination (Javorska et al., 2016), the current review gives a clear and concise overview of the novel or improved methods, focusing on 2014-2017, for vancomycin and/or teicoplanin quantification in different matrices.

The main aim in developing any analytical method is achieving good selectivity, sensitivity and extraction efficiency, which requires an efficient sample preparation method. Removing matrix components is required in order to minimize or eliminate the matrix effect in liquid chromatography-tandem mass spectrometry (LC-MS/MS) procedures, which have recently become more popular. Matrix components influence the ionization efficiency in the ionization source, reducing the sensitivity of the method. Techniques commonly used for sample preparation include protein precipitation (PP), liquid-liquid extraction (LLE) solid-phase extraction (SPE), and in this review their application for sample treatment for the two glycopeptide antibiotics is presented (Javorska et al., 2017; Begou et al., 2017; Kim et al., 2016; Sheng & Zhou, 2017; Brozmanová et al., 2017; Wicha & Kloft, 2016; Oyaert et al., 2015; Cao et al., 2014; Cazorla-Reyes et al., 2014; Zhang, 2014a; Zhang et al., 2014b; Bijleveld et al., 2014; Li et al., 2014).

Analytical methods

Protein precipitation. Protein precipitation is a simple, cost-effective, efficient, and time-saving method which includes removing proteins from the sample by denaturing them with appropriate organic solvent or acid followed by centrifugation. Protein precipitation was the method of choice for preparation of samples containing vancomycin or teicoplanin (Javorska et al., 2017; Begou et al., 2017; Sheng & Zhou, 2017; Brozmanová et al., 2017; Wicha & Kloft, 2016; Oyaert et al., 2015; Cao et al., 2014; Zhang et al., 2014b; Bijleveld et al., 2014; Cazorla-Reyes et al., 2014). Acetonitrile is frequently used as a precipitation agent for preparing plasma, serum, urine or peritoneal/pleural effusion containing vancomycin, and plasma or serum containing teicoplanin, giving a good extract purity (Oyaert et al., 2015; Cao et al., 2014, Javorska et al., 2017; Cazorla-Reyes et al., 2014, Begou et al., 2017; Cazorla-Reyes et al., 2014). However, acetonitrile did not achieve sufficient recovery for vancomycin determination in plasma or serum (Cao et al., 2014; Cazorla-Reyes et al., 2014). On the other hand, high recovery was obtained for vancomycin determination in low volumes of plasma, serum, urine or peritoneal/pleural effusion using acetonitrile as precipitation agent (Oyaert et al., 2015, Javorska et al., 2017). Namely, Begou et al (2017) investigated optimal deproteinization and extraction protocol from plasma in order to obtain high extraction recovery for all six teicoplanin components. Two different solvents (acetonitrile and methanol) in various volume ratios and using a low sample volume were tested. The highest recovery (more than 80%) was reached using ice-cold acetonitrile in a 3/1 (v/v) ratio. All other investigated combinations gave lower recoveries (Begou et al., 2017). Also, trichloroacetic acid can be applied as a precipitation agent for extraction of vancomycin in plasma or serum (Sheng & Zhou, 2017; Bijleveld et al., 2014, Brozmanová et al., 2017). Poor extraction purity, and thus low recovery (65.6%), was achieved by applying 10% trichloroacetic acid for precipitation of proteins from human plasma containing vancomycin (Bijleveld et al., 2014). The application of 10% trichloroacetic acid in combination with acetonitrile resulted in much better extraction purity and high recovery (Sheng & Zhou, 2017). Serum samples were prepared using 33% trichloroacetic acid as a precipitation agent and 0.5 mol L^{-1} ammonium hydroxide in order to increase pH value (Brozmanová et al., 2017). Methanol as a protein precipitation agent was used for determination of vancomycin in human plasma, bone or fat tissue, where the extraction recovery was approximately 100%, and in bacterial growth medium (Zhang et al., 2014b; Wicha & Kloft, 2016). The main disadvantage of protein precipitation as a sample preparation method is that matrix components other than proteins can remain in the sample, so it is of great importance to find optimal precipitation agents, optimal values of centrifugation parameters, and sample:precipitation agent ratios.

Solid-phase extraction (SPE) Although the main advantage of the SPE procedure is that can be automated, in the previous three years, this was not implemented for samples that contained vancomycin and/or teicoplanin.

Direct injection. Direct injection is a cost-effective and time-saving method. However, the main disadvantage for direct injection of plasma samples is that conventional HPLC columns can be clogged by proteins such as albumin that can remain on the column. Recently, analytical columns have been designed to exclude proteins, so allowing smaller molecules to interact with the stationary phases. Direct injection was a method of choice for plasma preparation in order to determine teicoplanin concentrations (Kim et al., 2016). Also, the dilution effect of a buffer with various acidic additives, such as formic acid and ammonium formate, was determined. Dilution (10-fold) of plasma with deionized water containing 0.1% formic acid gave the desired sensitivity for the analysis of all six components of teicoplanin (Kim et al., 2016).

Ultrafiltration. This technique allows the separation of free and protein-bound drug using ultrafiltration tubes that contain membrane with a molecular weight limit. Although therapeutic drug monitoring is based on total drug concentration in plasma or serum, for vancomycin, only that proportion which remains non-protein-bound is responsible for the antimicrobial activity. Zhang et al. (2014a) investigated the influence of the total protein levels and plasma osmotic pressure on the volume ratio of the ultrafiltrate to sample and on the free vancomycin level. In order to resolve this problem, hollow fiber centrifugal ultrafiltration was applied. This method could be successfully implemented in practice because of the results that it could give. Its main disadvantage is complexity of handling (Li et al., 2014; Zhang, 2014a).

Liquid-liquid extraction (LLQ). LLQ was often used in the past after protein precipitation for the analysis of vancomycin. On the other hand, in recent years, LLQ has not been utilized for determination of vancomycin and/or teicoplanin because of the toxic solvents that were used and the difficulty of automation (Cao et al., 2014).

Sample types, volumes and preparation methods for determining vancomycin and/or teicoplanin published mainly in the last three years are summarized in Table 1.

The coupling of LC with the excellent sensitivity and specificity of MS is a combination that allows more definitive identifications, and quantitative determinations of compounds that are not fully resolved chromatographically.

Different suitable C18 stationary phases are selected taking into account the nature of the investigated substances. High sensitivity and short analysis time is allowed by using an ultra performance liquid chromatography (UPLC) column for determination of vancomycin and simultaneous determination of teicoplanin and vancomycin (Brozmanová et al., 2017, Cazorla-Reyes et al., 2014). Special attention was paid to a UPLC-HILIC (hydrophilic interaction liquid chromatography) column that was utilized for vancomycin determination. HILIC mode, because of its high polarity and hydrophilicity, is especially convenient for vancomycin determination (Oyaert et al., 2015). Also, the high content of organic solvent, which is required for HILIC mode, is of great importance for MS detection in order to achieve better sensitivity. An overview of the columns utilized is given in Table 1.

For determination of vancomycin and teicoplanin, isocratic or gradient elution modes have been applied (Zhang et al., 2014a, Javorska et al., 2017; Begou et al., 2017; Sheng & Zhou, 2017; Brozmanová et al., 2017; Kim et al., 2016; Wicha & Kloft, 2016; Oyaert et al., 2015; Cao et al., 2014; Zhang et al., 2014b; Bijleveld et al., 2014; Li et al., 2014; Cazorla-Reyes et al., 2014). In isocratic mode, phosphate buffer was mixed with acetonitrile for the analysis of vancomycin, and analysis time was 10 min (Zhang et al., 2014a). In recent years, isocratic elution mode has not been the preferred elution method, as gradient elution more successfully eliminates endogenous compounds from samples containing vancomycin or teicoplanin, and so has become much more common. The gradient elution mode allows the use of a high content of organic solvent that is more suitable for MS detection. The most frequently used organic solvent in gradient mode for quantitative determination of vancomycin and/or teicoplanin is acetonitrile, but some authors reported use of methanol for analysis of these two drugs (Javorska et al., 2017; Begou et al., 2017; Sheng & Zhou, 2017; Brozmanová et al.; 2017; Kim et al., 2016; Wicha & Kloft, 2016; Oyaert et al., 2015; Cao et al., 2014; Bijleveld et al., 2014; Li et al., 2014; Zhang, 2014aZhang et al., 2014b; Cazorla-Reyes et al., 2014). In most cases, the aqueous phase consisted of water with different contents of formic acid (0.01-0.1%) (Javorska et al., 2017; Begou et al., 2017; Kim et al., 2016; Wicha & Kloft, 2016; Oyaert et al., 2015; Cazorla-Reyes et al., 2014; Zhang et al., 2014a; Zhang et al., 2014b; Li et al., 2014;). Also, it was reported that the aqueous phase could contain phosphate and ammonium acetate buffer (Cao et al., 2014; Sheng & Zhou, 2017; Brozmanová et al., 2017; Bijleveld et al., 2014; Li et al., 2014). Different gradient elution programs were implemented with various ratios of organic solvent to aqueous phase. The mobile phase compositions and types of elution mode are presented in Table 1.

According to literature published in the last three years, there are no published methods for analysis of teicoplanin that utilize UV detection. In the case of vancomycin analysis, there are three studies dealing with the LC method that used UV detection detection, UV detection is less sensitive and selective, so (Cao et al., 2014; Li et al., 2014; Zhang, 2014a). The detection wavelength was between 230 nm and 282 nm. However, compared with MS most methods for vancomycin and/or teicoplanin determination utilize MS detection.

Nowadays, LC-MS/MS is the method of choice for the analysis of vancomycin and all six components of teicoplanin in biological matrices. Vancomycin and teicoplanin are polypeptide structures, so the positive electrospray ionization (ESI) mode was selected in all recently published studies. For most polar compounds of high molecular weights, ESI is the first choice (Kazakevich, 2007). Large molecules with several ionizable sites, including teicoplanin and vancomycin, produce multiply-charged ions by ESI. All of the six components of teicoplanin and vancomycin were ionized as doubly charged molecular ions $[M+2H]^{2+}$ (Tsai et al., 2013). Teicoplanin A2-2/A2-3 (isomers 1) and teicoplanin A2-4/A2-5 (isomers 2) are isomer pairs with the same fragmentation, mass

Table 1. Chromatographic techniques and methods for detection of vancomycin and/or teicoplanin in biological matrices

Analyte	Matrix	Sample procedure	Column	Mobile phase composition	Recovery	Linearity range (μg mL^{-1})	t_R (min)	Internal standard	Type of detection	Reference
Vancomycin	Human serum	Protein precipitation (ACN)	Acquity BEH C18 (50 x 2.1 mm, 1.7 μm)	Gradient elution KH_2PO_4 (0.005 mol L^{-1}, pH 2.5) and ACN	62.9%	1-100	2.6	*p*-aminobenzoic acid	PDA 230 nm	Svetitsky, 2009
Vancomycin	Human plasma, bone, fat tissue	Protein precipitation (MeOH)	Luna C18 (50 x 2.1 mm, 5 μm)	Gradient elution 0.05% formic acid in water and MeOH	100%	0.05-50	2.4	Aminopterin	MS/MS	Zhang, 2014b
Vancomycin	Human plasma	Protein precipitation (ACN)	Acquity UPLC BEH HILIC (100 x 2.1 mm, 1.7 μm)	Gradient elution 0.1% formic acid in water and ACN	106.3%	0.3-100	2.7	Vancomycin-des-leucin	MS/MS	Oyaert et al., 2015
Vancomycin	Human plasma	Protein percipitation (10% TCA)	Hypurity Aquastar (100 x 2.1 mm, 1.7 μm)	Gradient elution Water, ACN, 0.2 mol L^{-1} perfluoropentanoic acid and 0.13 mol L^{-1} $NH_4C_2H_3O_2$ in water	65.6%	1-100	3.1	Kanamycin B	MS/MS	Bijleveld et al., 2014
Vancomycin	Human plasma	Ultrafiltration	Aston C18 (100 x 4.6 mm, 5 μm), capture column-Aston SCX (20 x 4.6 mm, 5 μm) and ACR C18 (250 x 4.6 mm, 5 μm)	Gradient elution 0.01 mol L^{-1} $NH_4C_2H_3O_2$ buffer and ACN (90/10, v/v, pH 3.8) 0.01 mol L^{-1} $NH_4C_2H_3O_2$ buffer in water pH 3 mol L^{-1} $NH_4C_2H_3O_2$ buffer and ACN (82.5/17.5, v/v, pH 5.2)	89.6-95.8%	0.2-49.9	8.5	/	UV 282 nm	Li et al., 2014
Vancomycin	Human plasma	Ultrafiltration	Diamonosil C18 (150 x 4.6 mm, 5 μm)	Isocratic elution MeOH and KH_2PO_4 (0.005 mol L^{-1}, pH 3.2)	/	0.25-50 (free form of vancomycin)	10.0	/	UV 236 nm	Zhang, 2014a
Vancomycin	Human serum, urine and peritoneal/ pleural effusion	Protein precipitation ACN	Meteoric Core C18 BIO column (100 × 4.6mm, 2.7 μm)	Gradient elution 0.1% formic acid in water and ACN	89 -104%	0.72-14.49 for serum, 2.898-86.94 for peritoneal/pleural effusion and 36.23-434.70 for urine	Total analysis time 4.5	Teicoplanin	MS/MS	Javorska et al., 2017

Analyte	Matrix	Sample procedure	Column	Mobile phase composition	Recovery	Linearity range (μg mL^{-1})	t_R (min)	Internal standard	Type of detection	Reference
Teicoplanin	Human plasma	Protein precipitation Cold ACN	Acquity BEH C18 column(150 × 2.1 mm 1.7 μm Acquity BEHC18 VanGuard pre-column (5 × 2.1 mm, 1.7 μm;	Gradient elution 0.1% formic acid in water and 0.1% formic acid in ACN	85-104%	0.025-6.4	2.2-2.8	Daptomycin	MS/MS	Begou et al., 2017
Teicoplanin	Human plasma	Direct injection	Cadenza HS-C18 analytical column(75 × 3.0 mm, 3 μm)	Gradient elution 0.1% formic acid in water and 0.1% formic acid in ACN	95.46-99.83	1–50	3.5	Sulfametho-xazole	MS/MS	Kim et al., 2016
Teicoplanin, vancomycin	Urine, serum, cerebrospinal fluid, bronchial aspirations	Protein precipitation (ACN) and dilution	Acquity UPLC BEH C18 column (100 ×2.1 mm, 1.7 μm	Gradient elution 0.01% formic acid in water and MeOH	70-86%	0.50-1.00 for urine 0.04-1.00 for serum 0.01-1.00 Ffor CSF 0.01-0.66 bronchial aspirations	2.6–2.7 for teicoplanin 0.7 for vancomycin	/	MS/MS	Cazorla-Reyes et al., 2014
Vancomycin	Bacterial growth medium	Precipitation (MeOH) with direct injection	AccucoreC18 (100 × 2.1 mm, 2.6 μm)	Gradient elution Water with 0.1% TFA and ACN	71%	0.2 -10	8.2	……/	DAD-3000 diode array detector 251, 240 and 302 nm	Wicha & Kloft, 2016
Vancomycin	Human plasma	Protein precipitation 10% TCA–ACN	Inertsil ODS-3 column (150×4.6 mm, 5 μm)	Gradient elution 20 mmol L^{-1} ammonium acetate buffer (pH 4.0) and ACN (88:12, v/v), deionized water, 50.0 mmol L^{-1} ammonium acetate buffer (pH 5.0) and ACN (85:15, v/v)	97.5-98.9	0.3–48.3	1.5	/	UV 282 nm	Sheng & Zhou, 2017
Vancomycin	Serum	33% TCA and 0.5 mol/L NH_4OH	Acquity UPLC BEH C18 column (50 ×2.1 mm, 1.7 μm	Gradient elution Buffer A (2 mmol/L ammonium acetate, 0.1% formic acid in 5% ACN v/v/v) and Buffer B (2 mmol/L ammonium acetate, 0.1% formic acid in 95% MeOH v/v/v)	98.7-102	0.1-100	0.7	Tobramycin	MS/MS	(Brozmanová et al., 2017

Note: ACN – acetonitrile; MeOH – methanol; TCA – trichloroacetic acid; TFA – trifluoroacetic acid

spectrometry parameter values, and chromatographic behavior and in the analysis were detected as two peaks.

Considering the previously mentioned facts about the mobile phase composition, in all published studies regarding vancomycin and teicoplanin determination, the addition of formic acid in the mobile phase and in samples preparation were described in order to achieve the desired protonation and good ionization efficiency.

The use of an internal standard is desirable to improve precision and accuracy. For MS methods, it is possible to use an isotopically labeled compound as an internal standard (Hoffmann, 2007). For vancomycin determination, vancomycin-des-leucine was used as an internal standard (Oyaert et al., 2015). Although isotopically-labeled internal standards are commercially available, high prices limit their use. The internal standards used in the previous three years for LC-MS/MS method development for vancomycin and/or teicoplanin determination are given in Table 1.

Also, among the published studies, a cost-effective system of two-dimensional liquid chromatography with ultraviolet detection (2D-LC-UV) for measurement of vancomycin in human plasma was reported. This method combines the automation of immunoassay with the high selectivity and sensitivity of LC coupled with MS detection (Sheng & Zhou, 2017; Li et al., 2014).

CONCLUSION

In this mini-review, sample preparation procedures and chromatographic methods for determination of vancomycin and/or teicoplanin are briefly presented with the emphasis on advantages and disadvantages of their properties. In the last three years, protein precipitation has become the most frequently used method for preparation of samples that contain vancomycin, teicoplanin or both. In order to reduce sample preparation time, there are efforts to automate sample preparation and to directly inject extracted sample into the LC-MS/MS system. Different LC–MS/MS methods have been described for quantitative determination of vancomycin and/or teicoplanin in various matrices. LC-MS/MS techniques are increasingly widely applied in clinical practice for measurement of these two drugs.

Acknowledgements

The authors thank the Ministry of Education, Science and Technological Development of the Republic of Serbia for supporting this investigation in Project 172052.

Authors' contributions

Authors have same contribution in manuscript preparation.

Declaration of conflicting interests

Hereby we disclose any financial and personal relationships with other people or organisations that could inappropriately influence our work.

REFERENCES

Begou O., Kontou A., Raikos N., Sarafidis K., Roilides E., Papadoyannis I. N., Gika H. G. 2017. An ultra-high pressure liquid chromatography-tandem mass spectrometry method for the quantification of teicoplanin in plasma of neonates. Journal of Chromatography B, 215. doi: 10.1016/j.jchromb.2016.01.042

Bijleveld Y., de Haan T., Toersche J., Jorjani S., van der Lee J., Groenendaal F., Dijk P., van Heijst A., Gavilanes A. W. D., de Jonge R., Dijkman K. P., van Straaten H., Rijken M., Zonnenberg I., Cools F., Nuytemans D., Mathôt R. 2014. A simple quantitative method analysing amikacin, gentamicin, and vancomycin levels in human newborn plasma using ion-pair liquid chromatography/tandem mass spectrometry and its applicability to a clinical study. Journal of Chromatography B, 951-952, 110-118. doi: 10.1016/j.jchromb.2014.01.035

Brozmanová H., Kacířová I., Uřinovská R., Šištík P., Grundmann M. 2017. New liquid chromatography-tandem mass spectrometry method for routine TDM of vancomycin in patients with both normal and impaired renal functions and comparison with results of polarization fluoroimmunoassay in light of varying creatinine concentrations. Clinica Chimica Acta, 469, 136-143. doi: 10.1016/j.cca.2017.04.003

Cao Y., Yu J., Chen Y., Zhang J., Wu X., Zhang Y., Li G. 2014. Development and validation of a new ultra-performance liquid chromatographic method for vancomycin assay in serum and its application to therapeutic drug monitoring. Therapeutic Drug Monitoring, 36(2), 175-181. doi: 10.1097/FTD.0b013e3182a458bc

Cazorla-Reyes R., Romero-González R., Frenich A.G., Martínez Vidal J. L., Rodríguez Maresca M. A. 2014. Simultaneous analysis of antibiotics in biological samples by ultra high performance liquid chromatography-tandem mass spectrometry. Journal of Pharmaceutical and Biomedical Analysis, 89, 203-212. doi: 10.1016/j.jpba.2013.11.004

Levine, D.P. 2006. Vancomycin: a history. Clinical Infectious Diseases, S5.

Hoffmann E. V. S. 2007. *Mass Spectrometry: principles and applications* (third ed.): John Wiley & Sons, England.

Javorska L., Krcmova L. K., Solich P., Kaska M. 2017. Simple and rapid quantification of vancomycin in serum, urine and peritoneal/pleural effusion via UHPLC–MS/MS applicable to personalized antibiotic dosing research. Journal of Pharmaceutical and Biomedical Analysis, 142, 59-65. doi: 10.1016/j.jpba.2017.04.029

Javorska L., Krcmova L. K., Solichova D., Solich P., Kaska M. 2016. Modern methods for vancomycin determination in biological fluids by methods based on high-performance liquid chromatography – A review. Journal of Separation Science(1), 6. doi: 10.1002/jssc.201500600

Jyoti T., Shrayanee D., Zeeshan F., Saif H. 2014. Multidrug resistance: an emerging crisis. Interdisciplinary Perspectives on Infectious Diseases, 2014, 1-7. doi: 10.1155/2014/541340

Kang H. K., Park Y. 2015. Glycopeptide antibiotics: Structure and mechanisms of action. Journal of Bacteriology and Virology, 45(2), 67-78. doi: 10.4167/jbv.2015.45.2

Kazakevich Y R. L. 2007. *HPLC for pharmaceutical scientists* (second ed.): John Wiley & Sons, New Jersey.

Kim K.-Y., Cho S.-H., Song Y.-H., Nam M.-S., Kim C.-W. 2016. Direct injection LC–MS/MS method for the determination of teicoplanin in human plasma. Journal of Chromatography B, 1008, 125-131. doi: 10.1016/j.jchromb.2015.11.037

Li X., Wang F., Xu B., Yu X., Yang Y., Zhang L., Li H. 2014. Determination of the free and total concentrations of vancomycin by two-dimensional liquid chromatography and its application in elderly patients. Journal of Chromatography B, 969, 181-189. doi: 10.1016/j.jchromb.2014.08.002

Vila M.M.D.C., Machado de Oliveira R., Gonçalves M.M., Tubino M. 2007. Analytical methods for vancomycin determination in biological fluids and in pharmaceuticals. Química Nova(2), 30, 395-399. doi: 10.1590/S0100-40422007000200029

Oyaert M., Peersman N., Kieffer D., Deiteren K., Smits A., Allegaert K., Spriet I., Van Eldere J., Verhaegen J., Vermeersch P., Pauwels S. 2015. Novel LC–MS/MS method for plasma vancomycin: Comparison with immunoassays and clinical impact. Clinica Chimica Acta, 441, 63-70. doi: 10.1016/j.cca.2014.12.012

Poonam Sood L., Juhi T., Bibhabati M. 2010. Methicillin and vancomycin resistant S. aureus in hospitalized patients. Journal of Global Infectious Diseases, 2(3), 275-283. doi: 10.4103/0974-777X.68535

Sheng Y., Zhou B. 2017. High-throughput determination of vancomycin in human plasma by a cost-effective system of two-dimensional liquid chromatography. Journal of Chromatography A, 1499, 48-56. doi: 10.1016/j.chroma.2017.02.061

Svetitsky S., Leibovici, L., & Paul, M. 2009. Comparative efficacy and safety of vancomycin versus teicoplanin: Systematic review and meta-analysis. Antimicrobial Agents And Chemotherapy, 53(10), 4069-4079.

Tsai I. L., Sun H.-Y., Chen G.-Y., Lin S.-W., Kuo C.-H. 2013. Simultaneous quantification of antimicrobial agents for multidrug-resistant bacterial infections in human plasma by ultra-high-pressure liquid chromatography–tandem mass spectrometry. Talanta, 116, 593-603. doi: 10.1016/j.talanta.2013.07.043

Wicha S. G., Kloft C. 2016. Simultaneous determination and stability studies of linezolid, meropenem and vancomycin in bacterial growth medium by high-performance liquid chromatography. Journal of Chromatography B, 1028, 242-248. doi: 10.1016/j.jchromb.2016.06.033

Zhang J., Yang, X., Zhang, Z., Dong, W., & Jiang, Y. 2014a. Accuracy of the analysis of free vancomycin concentration by ultrafiltration in various disease states. RSC Advances, 4(76), 40214-40222.

Zhang M., Moore, G. A., & Young, S. W. 2014b. Determination of vancomycin in human plasma, bone and fat by liquid chromatography/tandem mass spectrometry. Journal of Analytical & Bioanalytical Techniques, 5(3), 1-9. doi: 10.4172/2155-9872.1000196

PREGLED ANALITIČKIH METODA ZA ODREĐIVANJE VANKOMICINA I TEIKOPLANINA U BIOLOŠKOM MATERIJALU

STAJIĆ Ana, JANČIĆ-STOJANOVIĆ Biljana

Kratak sadržaj

Uvod. Teikoplanin i vankomicin su antibiotici glikopeptidne strukture koji se trenutno koriste u terapiji multirezistentnih bakterijskih infekcija.

Cilj i pristup. Ozbiljni neželjeni efekti vankomicina i teikoplanina kao što su ototoksičnost, nefrotoksičnost i neutropenija zahtevaju njihovo praćenje u različitim tipovima biološkog materijala. Osetljiva, pouzdana i brza metoda potrebna je u cilju dobijanja tačnih i preciznih podataka o koncentraciji pomenutih jedinjenja. Cilj ovog pregleda je da da jasan i kratak prikaz o razvijenim i validiranim novim, ili unapređenim metodama za analizu glikopeptidnih antibiotika u različitim biološkim matriksima. Takođe, u radu su opisane i metode pripreme uzorka upravo zbog raznovrsnosti biološkog materijala.

Ključni nalazi i zaključak. Opisane su raznovrsne LC-MS/MS metode za određivanje glikopeptidnih antibiotika u biološkom materijalu. Primećeno je da je precipitacija proteina pogodna metoda pripreme uzorka bez obzira na broj novijih metoda pripreme koje se koriste.

Ključne reči: Vankomicin, teikoplanin, uzorci biološkog materijala, određivanje, LC-MS/MS