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DEVELOPMENT AND VALIDATION OF THE IODOMETRIC METHOD FOR THE QUANTITATIVE DETERMINATION OF AMOXICILLIN

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РОЗРОБКА ТА ВАЛІДАЦІЯ КІЛЬКІСНОГО ВИЗНАЧЕННЯ АМОКСИЦИЛІНУ ЙОДОМЕТРИЧНИМ МЕТОДОМ

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Abstract

Background. *The development of new methods for quantitative determination of penicillin's remains relevant. The developed method of quantitative determination of Amoxicillin can be used to develop analytical regulatory documentation for medicinal products, as well as in the practice of state laboratories for quality control of medicinal products and central factory laboratories of pharmaceutical enterprises. Purpose. Development of new improved unified method for the quantitative determination of Amoxicillin (Amox) by redox titration.* ***Materials and Methods.*** *The object of the study was Amox sodium powder in vials for the preparation of an injection solution («Amoxicillin Sodium Salt», 1000 mg). Peroxomonosulfate acid as triple potassium salt $2KHSO_5 \cdot KHSO_4 \cdot K_2SO_4$ (Oxone®) of "extra pure" qualification was used as oxidant. The redox titration method was used to develop a method for the quantitative determination of amoxicillin in a substance and a medicinal product using potassium caroate as an analytical reagent ($KHSO_5$).* ***Results.*** *The kinetics and stoichiometry of the S-oxidation reaction of Amox with potassium caroate in aqueous solutions were investigated by iodometric titration. A unified methodology was developed and the possibility of qualitative determination of Amox in pure substance and drug using potassium caroate was investigated by redox titration method. At pH 2-4 for 1 mole of penicillin, 1 mole of $KHSO_5$ is consumed, the quantitative interaction is achieved within a time of more than 1 minute (observation time). The results obtained according to the recommended procedure for seven repeated titrations of mixtures of different concentrations. RSD = 0.85%, δ = (+ 0.16)%.* ***Conclusions.*** *Using the redox titration method, a method for the quantitative determination of Amox in the substance was developed and the drug product have been developed using potassium caroate as an analytical reagent ($KHSO_5$). The possibility of analytical determination of Amox by the biologically active part of the molecule is shown, the proposed methods give reproducible and accurate results.*

Key words: oxidation, redox titration method, validation, potassium caroate, amoxicillin.

Анотація

Актуальність. *Розробка нових методик кількісного визначення пеніцилінів залишається актуальною. Розроблена нова методика кількісного визначення амоксициліну може бути використана для розробки аналітичної нормативної документації на лікарські засоби, а також у практиці державних лабораторій з контролю якості лікарських засобів та центральних заводських лабораторій фармацевтичних підприємств.* ***Мета роботи.*** *Розробка нової вдосконаленої уніфікованої методики кількісного визначення амоксициліну методом окисно-відновного титрування.* ***Матеріали та методи****. Об'єктом дослідження був порошок натрій амоксициліну у флаконах для приготування розчину для ін'єкцій («Амоксициліну натрієва сіль», 1000 мг). Як окисник використовували пероксомоносульфатну кислоту у вигляді потрійної калієвої солі $2KHSO_5 \cdot KHSO_4 \cdot K_2SO_4$ кваліфікації "extra pure" (Oxone®). Використовували метод окисно-відновного титрування для розроблення методики кількісного визначення амоксициліну в субстанції та лікарському засобі з використанням калій кароату як аналітичного реагенту ($KHSO_5$).* ***Результати та їх обговорення.*** *Було досліджено кінетику та стехіометрію реакції S-окиснення амоксициліну за допомогою калій кароату у водних розчинах методом йодометричного титрування. Розроблено уніфіковану методику та досліджено можливість кількісного визначення методом окисно-відновного титрування амоксициліну в чистій речовині субстанції та препараті з використанням калій кароату. При pH 2-4 на 1 моль пеніциліну витрачається 1 моль $KHSO_5$, кількісна взаємодія досягається протягом 1 хвилини (час спостереження). Результати отримані згідно з рекомендованою процедурою для семи повторних титрувань сумішей різної концентрації. RSD = 0.85%, δ = (+ 0.16)%.* ***Висновки.*** *Використовуючи метод окисно-відновного титрування,*

була розроблена методика кількісного визначення амоксициліну в субстанції та лікарському засобі з використанням калій кароату як аналітичного реагенту ($KHSO_5$). Показано можливість аналітичного визначення амоксициліну за біологічно активною частиною молекули, запропонована методика має високу відтворюваність та точність результатів.

Ключові слова: *окиснення, окисно-відновне титрування, валідація, калій кароат, амоксицилін.*

1. Introduction

The defining feature of penicillins is their core structure, known as the penicillin nucleus or 6-aminopenicillanic acid (6-APA), which consists of a β-lactam ring fused to a thiazolidine ring, and this unique bicyclic system is essential for their antibacterial action by interfering with bacterial cell wall synthesis. Amoxicillin (Amox) is a type of penicillin antibiotic. It's used to treat bacterial infections, such as chest infections (including pneumonia) and dental abscesses. It can also be used together with other antibiotics and medicines to treat stomach ulcers. The IUPAC name for Amox is sodium (indicates it's the sodium salt form) (2S,5R,6R)-6-[[(2R)-2-amino-2-(4-hydroxyphenyl)acetyl]amino]-3,3-dimethyl-7-oxo-4-thia-1-azabicycloheptane-2-carboxylate, a precise chemical description of its complex structure, highlighting the sodium ion and the specific stereochemistry (2S, 5R, 6R, 2R) of the Amox molecule, with its thiazolidine and beta-lactam rings, linking to the hydroxyphenylglycine side chain. Amox, an acid stable, semisynthetic drug belongs to a class of antibiotics called the Penicillins. It is shown to be effective against a wide range of infections caused by wide range of gram-positive and gram-negative bacteria. Amox is an aminopenicillin created by adding an extra amino group to penicillin to battle antibiotic resistance. This drug is indicated for the treatment of infections caused by susceptible isolates of selected bacteria, specifically those that are beta-lactamase–negative, including ear, nose, and throat infections, Helicobacter pylori eradication, lower respiratory and urinary tract infections, acute bacterial sinusitis, and skin and structure infections [2].

In a highly acidic environment, penicillins undergo a number of chemical reactions that lead to the formation of inactive decomposition products. Fig. 1 shows the first stage, Penicilloic acid is formed. The process is initiated by protonation of the nitrogen atom of the lactam ring.

β-Lactam antibiotics (BLAs) are among the most important and widely used antimicrobials worldwide and are comprised of a large family of compounds, obtained by chemical modifications of the common scaffolds. Usually, these modifications include the addition of active groups, but less frequently, molecules were synthesized in which either two β-lactam rings were joined to create a single bifunctional compound, or the azetidinone ring was joined to another antibiotic scaffold or another molecule with a different activity, in order to create a molecule bearing two different pharmacophoric functions. Fig. 2 shows another hydrolysis pathway for the conversion of penicillic acid to penylic acid with subsequent decarboxylation and hydrolytic ring opening and the formation of penylic acid [8].

Penicillins are a type of β-lactam antibiotic consisting of a four-membered β-lactam ring bound to a five-membered thiazolidine ring. This two-ring system causes distortion of the β-lactam amide bond, resulting in decreased resonance stabilization and increased reactivity. β-lactams inhibit the formation of peptidoglycan cross-links within bacterial cell walls by targeting penicillin-binding proteins or PBPs. Consequently, the bacterial cell wall becomes weak and cytolysis occurs. Resistance to β-lactam antibiotics occurs in the presence of cells containing plasmid

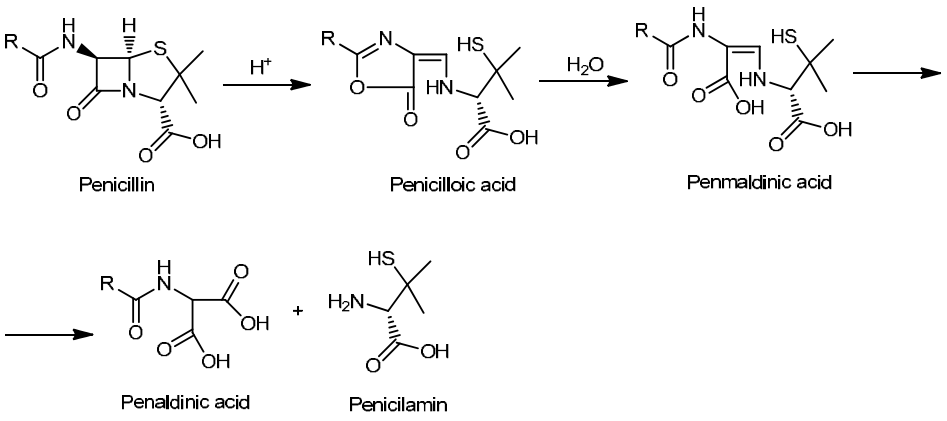

Fig. 1. Stages of formation Penaldinic acid and Penicilamin

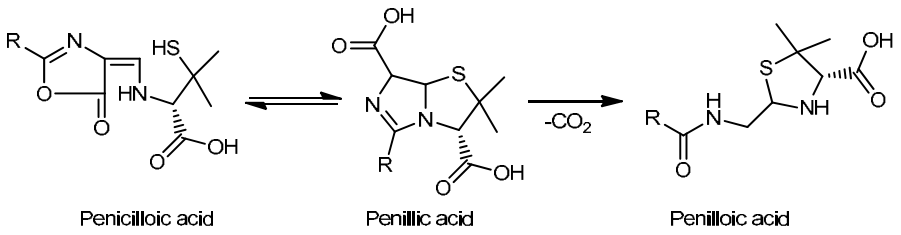

Fig. 2. Stages of formation Penilloic acid

encoded extended spectrum β-lactamases or ESBLs. Antibiotics are often used in clinical in vitro tests known as antimicrobial susceptibility tests or ASTs to determine their efficacy against certain bacterial species. They are tested against gram-negative and gram-positive bacteria using panels, discs, and MIC strips by medical microbiologists. ASTs decrease the risk of using an antibiotic against bacteria exhibiting resistance to it, and the results are used in clinical settings to determine which antibiotic(s) to prescribe for various infections [9].

The quantitative determination of drugs penicillin series becomes more and more important. The control of the quality and quantity is one of the obligatory steps for manufacturing medicines. The number of medicines produced increases from year to year and the quality of the drugs have to be controlled. Therefore, the development of new procedures that are easy to perform and cost-effective is of great interest. The procedures proposed should be unified, selective, sensitive, and precise, and they should be validated by the monograph "Validation of analytical methods" of the State Pharmacopeia of Ukraine (SPhU). European Pharmacopoeia (EPh) penicillin quantitative determination is performed by high performance liquid chromatography (HPLC). International Pharmacopoeia recommends to determine penicillin summary in semisynthetic penicillin by neutralization method after preparation hydrolysis by excess of sodium hydroxide titrated solution at heating [10].

The analysis of literary data shows that a promising direction of scientific research is to find out the possibility of carrying out the analysis of penicillins. The methods that are currently used to determine penicillins in pharmaceutical preparations have been reviewed. They include analytical measurement and appliance, equipment designed to perform a specific task in dependency of detection methods.

Iodometry is a type of redox (reduction-oxidation) titration. It is a method of volumetric chemical analysis that relies on the transfer of electrons between reacting species. Specifically, iodometry is an indirect redox titration method used to determine the concentration of an oxidizing agent in a solution.

The process involves two main steps that constitute the overall redox reaction:

Iodine Liberation. An excess amount of potassium iodide (KI) is added to a known volume of the sample containing the oxidizing agent (analyte). The oxidizing agent reacts with the iodide ions (I^-) to liberate a proportional amount of free iodine (I_2).

Titration. The liberated iodine is then titrated with a standard solution of a reducing agent, usually sodium thiosulfate ($Na_2S_2O_3$), using a starch indicator. The reaction consumes the iodine, and the endpoint is signaled by the disappearance of the characteristic deep blue color of the starch-iodine complex.

The amount of sodium thiosulfate used to consume the liberated iodine allows for the calculation of the original concentration of the oxidizing agent in the sample. Iodometry is distinct from iodimetry, which is a direct redox titration where a reducing agent (analyte) is directly titrated with a standard iodine solution. Both are subtypes of redox titrations. Classical iodometry of penicillin's hydrolysis products (penicilloic acids) is a recognized, basic, though lengthy, method for its quantitative determination, relying on the reaction of these products with excess iodine, which is then back-titrated with thiosulfate; it's a traditional redox titration used in pharmacopoeias, though modern, faster techniques (like spectrophotometry or enzyme sensors) exist, notes [11].

International Pharmacopoeia recommends to determine penicillin summary in semisynthetic penicillin by neutralization method after preparation hydrolysis by excess of sodium hydroxide titrated solution at heating. According to State Pharmacopoeia of Ukraine (SPhU) and European Pharmacopoeia (EPh) penicillin quantitative determination is performed by high performance liquid chromatography (HPLC). Well, described in scientific articles methods of potentiometry titration, amperometry, high-performance liquid chromatography (HPLC), voltammetry, polarographic analysis, micelle electrokinetic capillary, spectrophotometry, chemiluminescense, redox titration, electrophoresis and others [1, 3–7, 12–22] for

the quantitative determination of penicillin drugs.

The issue of quantitative determination of penicillins does not lose its relevance. Most of the known methods for the quantitative determination of penicillins are reduced to the determination of the final products of their hydrolytic cleavage, which are obtained at the previous stage of analysis. They are long-lasting and require heating.

Redox titrations can be used to quantify penicillin by oxidizing the antibiotic, often in a process that involves alkaline hydrolysis followed by reaction with an oxidizing agent like iodine or a potassium caroate ($KHSO_5$) based reagent. In an iodometric method, the penicillin is oxidized by iodine, and the amount of iodine consumed is determined indirectly by back-titrating with a reducing agent such as sodium thiosulfate. In methods using ($KHSO_5$), the penicillin is oxidized directly, and the amount of reagent used is determined by titration.

The developed redox titration method is time saving, simple, accurate, economic, sensitive and reproducible, can be used in quality control laboratories. Also, the principal advantages of the present method are that it is rapid and enough precise comparing with other methods of assay [23, 24].

2. Materials and methods

All the materials were of analytical reagent grade, and the solutions were prepared with double-distilled water.

For the research, Amoxicillin sodium salt of pharmacopoeial purity, a dry sterile powder in vials (1,0 g) for inejction «Amoxicillin Sodium Salt», CAS Number 34642-77-8, Catalog Number A-551-1, Jiangxi Bolai Pharmacy Co., Ltd, China. Potassium caroate was obtained from commercial sources and used as an oxidant in the form of a triple potassium salt ($2KHSO_5 \cdot KHSO_4 \cdot K_2SO_4$, "Oxone") of "extra pure" grade with an active oxygen content of 4.5%. The choice of the reagent was due to its availability, fairly good solubility and stability in aqueous solutions, and a relatively high oxidizing ability.

The reagent is used due to its availability, good solubility and stability in water, also its relatively high oxidation ability. Standard electrode potential for semireaction

$$HSO_5^- + 2H^+ + 2e^- \rightarrow HSO_4^- + H_2O$$

is 1.81 V.

As a standard sample of Amoxicillin sodium salt, we used the substance of Amox of pharmacopoeial purity with the content of the main substance of 98.5%.

Sodium thiosulfate solution, 2×10^{-2} mol·L^{-1}. An ampoule of a standard titer of sodium thiosulfate with an exact concentration of 0.1 mol·L^{-1} was diluted five times with distilled water.

Solution of potassium iodide, 5%. A weighed portion of 5.0 g of potassium iodide was dissolved in 50 mL of distilled water, and the solution was diluted to the volume in a 100 mL volumetric flask at 20 °C.

Sulfuric acid, 0.1 mol·L^{-1}. An ampoule of a standard titer of sulfuric acid with an exact concentration of 0.1 mol·L^{-1} was diluted with distilled water.

Solution of potassium caroate (0.02 mol/l) in water was prepared by dissolving 0.615 g of potassium caroate in double distilled water, transferring the solution into a 100-ml volumetric measuring flask, diluting to volume and mixing at +20 °C. Solution concentration is determined by iodometric titration. 10.00 ml of prepared solution was transferred to 100-ml measuring flask, diluted. 10.00 ml of prepared solution was transferred into titration flask, 1 ml of 0.1 mol·L^{-1} sulfuric acid solution and 1 ml of 5% potassium iodide were added. The excess of iodine was titrated with 2×10^{-2} mol/l sodium thiosulphate.

Titration. The titer of the Amox solution studied was determined using a 10 mL microburette with an accuracy of ± 0.01 mL filled with a titrant to the zero mark.

Redox titration method. Close 850 mg (accurate weight) of the powder of the Amox sodium salt studied was dissolved in 70 mL of water in a 100 mL volumetric flask at 20°C, and diluted to the volume. Using a pipette, 10 mL of the resulting Amox solution was taken and transferred to a 100 mL volumetric flask, 10.0 mL of a 2×10^{-2} mol·L^{-1} $KHSO_5$ solution was added with stirring, and diluted to the volume with distilled water at 20°C. Using a pipette, 10 mL of the reaction mixture was taken and transferred to a 100 mL flask, acidified with 1 mL of a 0.1 mol·L^{-1} H_2SO_4 solution, and 2 mL of a 5% potassium iodide solution was added with vigorous stirring. The displaced iodine was immediately titrated with a standard 2×10^{-2} mol·L^{-1} sodium thiosulfate solution. In parallel, under the same conditions, a control experiment is carried out (without the Amox solution studied).

3. Results and Discussion

By the method of reverse redox titration of $KHSO_5$ residue was determined that 1 mol of $KHSO_5$ is used per 1 mol of Amox. The reaction finishes during 1 min and stays for 30 min (observation time at pH 2-4). The transformation

scheme of analytical determination of Amox is given on Fig.3.

The content of $C_{16}H_{18}N_3NaO_5S$ (X, in%) was calculated by the formula:

$$X = \frac{0.02 \cdot K \cdot 387.39 \cdot (V_0 - V) \cdot 100 \cdot 100\%}{2 \cdot 1000 \cdot m_s \cdot (100 - w_{H_2O})},$$

where V_0 – is the volume of sodium thiosulfate solution in the control experiment, mL;
V – is the volume of sodium thiosulfate solution studied, mL;
387.39 – is the molar mass of Amoxicillin sodium salt anhydrous, g·mol^{-1};
K – is the correction coefficient for the concentration of sodium thiosulfate solution to 0.0200 mol·L^{-1};
m_s – is the weighed portions of Amox, g.

The results of the analysis of the Amox drug by redox titration are shown in Table 1. The relative standard deviation did not exceed 0.85% (δ = + 0.16%).

4. Conclusions

The possibility of analytical determination of Amox by the biologically active part of the molecule (alicyclic sulfur and β-lactam ring) is shown, the proposed methods give reproducible and accurate results. The developed method have good specificity and allow determining the content of the main component of Amox, avoiding the influence of impurities. The results of accuracy and precision are in good agreement with the results obtained by the reference method. Using the redox titration method, a method for the quantitative determination of Amox in the substance was developed and the drug product have been developed using potassium caroate as an analytical reagent ($KHSO_5$). The developed method of quantitative determination of Amox can be used to develop analytical regulatory documentation for medicinal products, as well as in the practice of state laboratories for quality control of medicinal products and central factory laboratories of pharmaceutical enterprises.

Перспективи подальших досліджень. У подальшому планується розробка нових методик кількісного визначення цілої низки пеніцилінів, які матимуть ряд переваг перед уже відомими: дадуть можливість визначати їх у значно менших кількостях, ніж фармакопейним методом йодометрії, що будуть придатні для того самого інтервалу визначуваних концентрацій.

Обмеження дослідження. Обмеження цього дослідження полягають у тому, що можуть бути використані тільки для препаратів пеніцилінового ряду, які за хімічною будовою є похідними 6-амінопеніцилятної кислоти (6-АПК) – конденсованої системи тіазолідинового і чотириланкового β-лактамового циклів, які різняться між собою радикалом R ацилу, з'єднаним з аміногрупою 6-АПК.

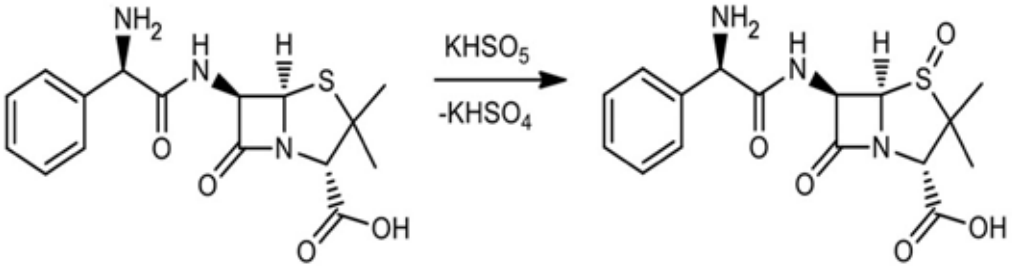

Fig. 3. The scheme of S-oxidation of Amox by potassium caroate

Table 1

Results of the quantitative determination of Amoxicillin by redox titration in the Amox drug by the reaction with potassium caroate (P = 0.95, n = 7)

Amoxicillin taken, mg	Found		Results of processing statistical data
	m	%	
935.0[a]	944.3	94.4	$\bar{x}$ = 936.5 (93.6%) S = ± 7.98906 S_x = ±3.01958 $\Delta\bar{x}$ = ± 7.39797 RSD = ± 0.85% ε = ± 0.79% δ[b] = + 0.16%
	927.1	92.7	
	929.4	92.9	
	942.5	94.3	
	928.3	92.8	
	938.6	93.9	
	945.2	94.5	

Note: [a] The Amox content indicated in the quality certificate (μ); [b] δ = ($\bar{x}$–μ) × 100%×μ^{-1}

Конфлікт інтересів

Автори заявляють про відсутність будь-якого конфлікту інтересів (фінансового чи особистого), який міг би вплинути на результати, викладені в цій статті.

Використання штучного інтелекту

При написанні статті штучний інтелект не використовували в жодному з пунктів.

Первинні дані та матеріали

Основою для наукового **емпіричного** дослідження **є** результати лабораторних експериментів, вимірювань, відповідних розрахунків.

Інформація про фінансування

Це дослідження не отримало жодного конкретного гранту від фінансових організацій у державному, комерційному чи некомерційному секторах (самофінансування).

Внесок авторів

С. П. Карпова: розробка методики кількісного дослідження, збір літературних джерел, формулювання анотацій та висновків;

О. В. Антоненко: статистична обробка результатів, підготовка графіків та таблиць.

Разом автори проводили експериментальну частину, критично оформлювали зміст статті, схвалили остаточний варіант рукопису перед поданням до друку.

REFERENCES

1. Abdelrahman, M., Naguib, I., Elsayed, M. (2018). Chromatographic methods for quantitative determination of ampicillin, dicloxacillin and their impurity 6-aminopenicillanic acid. *Journal of Chromatography Science,* 56(3), 209–215. doi.org/10.1093/chromsci/bmx101.

2. Armoudjian, Y., Lin, Q., Lammens, B. (2023). Sensitive and rapid method for the quantitation of amoxicillin in minipig plasma and milk by LC-MS/MS: a contribution from the IMI ConcePTION project. *Journal of Pharmacological and Toxicological Methods*, 123, 107264. doi.org/10.1016/j.vascn.2023.107264.

3. Asan, A., Seddiq, N. (2022). A Simple spectrophotometric determination of amoxicillin in drug samples. *Journal of the Turkish Chemical Society*, 9(2), 423–432. doi.org/10.18596/jotcsa.978686.

4. Dubenska, L., Blazheyevskiy, M., Plotycya, S. (2017). Voltammetric methods for the determination of Prarmaceuticals. *Methods and Objects of Chemical Analysis*, 12(2), 61-75. doi.org/10.17721/moca.2017.61–75.

5. El-Desoky, H., Ghoneim, E., Ghoneim, M. (2005). Voltammetric behavior and assay of the antibiotic drug cefazolin sodium in bulk form and pharmaceutical formulation at a mercury electrode. *Journal of Pharmaceutical and Biomedical* Analysis, 39(5), 1051–1056. doi.org/10.1016/j.jpba.2005.05.020.

6. Fazelirad, H., Ranjbar, M., Taher, M.A. (2015). Preparation of magnetic multi-walled carbon nanotubes for an efficient adsorption and spectrophotometric determination of amoxicillin. *Journal of industrial and engineering* chemistry, 21. 889–892. doi.org/10.1016/j.jiec.2014.04.028.

7. Ismail, F., Adeloju, S. (2010). Galvanostatic entrapment of penicillinase into polytyramine films and its utilization for the potentiometric determination of penicillin. *Sensors*, 10(4), 2851–2868. doi.org/10.3390/s100402851.

8. Karpova, S., Zhuravel, I., Kolisnyk, S., Kryskiv, O., Krutskikh, T., Maslov, O. (2024). Analytical approach of kinetic-spectrophotometric and redox titration methods in the quantitative determination of ticarcillin. *Voprosy khimii i khimicheskoi tekhnologii*, 6, 81–88. doi.org/10.32434/0321-4095-2024-157-6-81-88.

9. Kaur, S., Rao, R., Nanda, S. (2011). Amoxicillin: a broad spectrum antibiotic. *International Journal of Pharmacy and Pharmaceutical Sciences*, 3(3), 30–37. www.researchgate.net/publication/304704877.

10. Keij, F.M., Schouwenburg, S., Kornelisse, R.F., Preijers, T., Mir, F. (2023). Oral and intravenous amoxicillin dosing recommendations in neonates: a pooled population pharmacokinetic study. *Clinical Infectious Diseases*, 77(11), 1595–1603. doi.org/10.1093/cid/ciad432.

11. Li, K., Mohammed, M., Zhou, Y. (2020). Recent progress in the development of immobilized penicillin G acylase for chemical and industrial applications: a mini-review. *Polymers for Advanced Technologies,* 31(3), 368–388. doi.org/10.1002/pat.4791.

12. Liu, Q., Liu, L., Yuan, Y., Xie, F. (2023). A validated UHPLC-MS/MS method to quantify eight antibiotics in quantitative dried blood spots in support of pharmacokinetic studies in neonates. *Antibiotics,* 12(2), 199. doi.org/10.3390/antibiotics12020199.

13. Matsumoto, H., Shiotani, A., Graham, D. (2019). Current and Future Treatment of Helicobacter pylori Infections. *Advances in Experimental Medicine and Biology*, 1149, 211–225. doi.org/10.1007/5584-2019-367.

14. Page-Sharp, M., Yoo, O., Salman, S., Davis, T. (2024). Validation and Application of a Dried Blood Spot Amoxicillin Assay. *Chromatographia,* 87, 493–501. doi.org/10.1007/s10337-024-04341-z.

15. Rosa, M., Verdino, A., Soriente, A. (2021). The odd couple(s): an overview of beta-lactam antibiotics bearing more than one pharmacophoric group. *International Journal of Molecular Sciences*, 22(2), 617–638. doi.org/10.3390/ijms22020617.

16. Rusu, A., Antonoaea, P., Ciurba, A. (2019). Development of a rapid capillary zone electrophoresis method to quantify levofloxacin and meloxicam from transdermal therapeutic systems. *Studia Universitatis Babes-Bolyai Chemia*, 64 (1), 219–231. doi.org/10.24193/subbchem.2019.1.18.

17. Simon, B., Hancu, G., Gyéresi, A. (2014). Application of capillary electrophoresis to the simultaneous determination and stability study of four extensively used penicillin derivatives. *Brazilian Journal of Pharmaceutical Sciences*, 50(3), 521–527. doi.org/10.1590/S1984-82502014000300010.

18. Soares, A.L., Montanha, M.C., Alcantara, CDS. (2021). Pharmacokinetics of amoxicillin in obese and nonobese subjects. *British Journal of Clinical Pharmacology*, 87(8), 3227–3233. doi.org/10.1111/bcp.14739.

19. Stredansky, M, Pizzariello, A, Stredanska, S. (2000). Amperometric pH-sensing biosensors for urea, penicillin, and oxaloacetate. *Analytica Chimica* Acta, 415(1-2), 151–157. doi.org/10.1016/S0003-2670(00)00869-2.

20. United States Pharmacopeial Convention, Rockville, Maryland. (2015), 4. https://search.worldcat.org/title/The-United-States-pharmacopeia-:-the-national-formulary/oclc/933365422.

21. Zhang S., Liao X., Ding T. (2024). Role of β-lactamase inhibitors as potentiators in antimicrobial chemotherapy targeting gram-negative bacteria. *Antibiotics*, 13(3), 260-280. doi.org/10.3390/antibiotics13030260.

22. Zhang, Y., Cui, G., Meng, Y., Wang, Y., Hun, X. (2021). Chemiluminescence assay for *Listeria monocytogenes* based on Cu/Co/Ni ternary nanocatalyst coupled with penicillin as generic capturing agent. *Luminescence*, 36(1), 11-19. doi.org/10.1002/bio.3908.

23. Zheng, F., Wang, S., Wen, S., Shen, M., Zhu, M., Shi, X. (2013). Characterization and antibacterial activity of amoxicillinloaded electrospun nano-hydroxyapatite/poly (lactic-coglycolic acid) composite nanofibers. *Biomaterials*, 34(4), 1402-1142. doi.org/10.1016/j.biomaterials.2012.10.071.

24. Zhou, Y., Gao, Y., Pang, S.Y., Jiang, J., Yang, Y., Ma, J., Guo, Q. (2018). Oxidation of fluoroquinolone antibiotics by peroxymonosulfate without activation: Kinetics, products, and antibacterial deactivation. Water Research, 145, 210-219. doi.org/10.1016/j.watres.2018.08.026.

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