Journal of Research in Pharmacy

Research Article

www.jrespharm.com

Design of a novel colorimetric method based on AuNPs for tazobactam and piperacillin detection

Zehra Ozden ERDOGAN [1] *, **Hakan BALCI** [1,2]

1 Pharmacy Services, Vocational School, Yuksek Ihtisas University, Ankara, Türkiye.
2 Department of Medical Pharmacology, Faculty of Medicine, Bilecik Seyh Edebali University, Bilecik, Türkiye.
* Corresponding Author. E-mail: duruzera@gmail.com (Z.O.E); Tel. +(+90 312) 3297425.

Received: 04 November 2023 / Revised: 21 January 2023 / Accepted: 30 January 2023

ABSTRACT: In the present paper, a colorimetric method for the determination of tazobactam and piperacillin based on plasmonic nanoparticles (AuNPs) is suggested. Plasmonic nanoparticles have gained interest for application in the creation of sensitive analytical techniques because of their unique features. The localized surface plasmon resonance (LSPR) absorption band for AuNPs with a wavelength 543.5 ($A_{543.5}$) nm was used for analysis. The working parameters such as the amount of AuNPs and pH were optimized to obtain the optimum experimental conditions. The calibration curve for the colorimetric method was prepared with tazobactam and piperacillin concentrations ranging from 2.25-30.04 mg/L and0.52-10.33 mg/L, respectively. The detection limits were found to be 1.01 mg/L for tazobactam and 0.29 mg/L for piperacillin The AuNPs-based colorimetric method suggested in this work can use as an alternative analytical method for routine analysis of tazobactam and piperacillin because it is quick, simple, and affordable.

KEYWORDS: AuNP; piperacillin; spectrophotometry; tazobactam

1. INTRODUCTION

Colorimetry is an analysis method that allows determining the content of the target analyte by comparing and/or measuring the color depth of solutions of colored substances. Compared to other analysis methods, colorimetry is more intuitive and results can be observed directly with the naked eye [1-3]. However, there are still challenges with colorimetric analysis methods that need to be resolved, including complexity, low sensitivity, and the requirement for large sample quantities. To overcome these limitations, nanoparticles (NP), nanorods, nanowires and other nanostructured materials (NM) with suitable chemical, physical and optical properties are used as a platform in colorimetric analysis methods [4-6]. In recent years, colorimetric methods based on nanomaterials have been developing rapidly and are widely used. The combination of nanomaterials and colorimetry brings a new perspective to colorimetry as it provides lower detection limits and high sensitivity [7]. Among nanomaterials, especially noble metal nanoparticles such as copper (Cu), silver (Ag) and gold (Au) attract a lot of attention due to their easy functionalization, biostability, and stable localized surface plasmon resonances (LSPR) in the UV-Vis region [8-10]. When these metal nanoparticles (MNP) interact with the electromagnetic wave, the electrons on the surface of the MNPs oscillate freely and exhibit an absorption band. These properties allow MNPs to be used as a detection probe in the quantitative determination of various chemical substances [11, 12]. Colorimetric analysis methods based on MNPs are used in various fields such as cancer and disease diagnosis [13, 14], drug therapy monitoring [15], drug targeting, drug development [16], food safety [17, 18], environmental monitoring [19], and biotechnology [20, 21].

Piperacillin is a semi-synthetic ureidopenicillin with antibacterial activity against gram positive and gram negative aerobic and anaerobic bacteria. In recent years, the clinical role of piperacillin has been put at risk as a result of the increasing prevalence of drug-resistant β-lactamase-producing bacteria. Tazobactam, a triazolilmethyl penicillanic acid sulfone derivative, is a β-lactamase inhibitor that protects piperacillin from β-lactamase enzymes. The use of piperacillin in combination with tazobactam broadens the spectrum and acts against many β-lactamase-producing bacteria such as Staphylococci, Enterobacteriaceae, Haemophilus influenzae and Bacteroides [22]. It is known that the piperacillin-tazobactam combination has good efficacy in intra-abdominal infections, urinary tract infections, gynecology and soft tissue infections caused by β-lactamase producing bacteria species. Nowadays, it is seen as a result of clinical findings that such pathogens are widespread throughout the world, and it is reported that the effect of the combination of tazobactam-

How to cite this article: Erdogan Z.O., Balci H. Design of a novel colorimetric method based on AuNPs for tazobactam and piperacillin detection. J Res Pharm. 2023; 27(3): 1066-1075.

http://dx.doi.org/10.29228/jrp.399

ISSN: 2630-6344

piperacillin used in the fight against these pathogens is dose-dependent [23-25]. Therefore, determining the plasma level of the piperacillin-tazobactam dose used against these infections will allow both to keep the drug dose in the therapeutic range and to prevent the development of drug resistance against β-lactamases synthesized by bacteria by reducing the side-effect profile. In addition, it is known that approximately 50% to 60% of the administered piperacillin-tazobactam dose is excreted via the kidney [26]. For this reason, knowing the clearance of the drug in urine is another important point in determining the amount of dose that should be administered to keep the drug in the therapeutic range in plasma.

This study aimed to develop a new colorimetric method for the determination of piperacillin and tazobactam using AuNPs. In line with this goal, the determination of the drugs at lower concentrations was carried out in order to reflect the clinic by utilizing the surface plasmon property of AuNPs.

2. RESULTS AND DISCUSSION

AuNPs, a plasmonic nanoparticle, were used as nanomaterial in the colorimetric determination of tazobactam and piperacillin. Due to their confined surface plasmon resonance property and high absorption extinction coefficient, AuNPs, which are commonly employed in colorimetric measurement, exhibit great sensitivity in analyses [7]. The absorbance ratios (Abstazo/AbsAuNPs and Abspip/AbsAuNPs) calculated using the SPR absorbance of AuNPs at 526.0 nm wavelength (Figure 1) were used in the analyses.

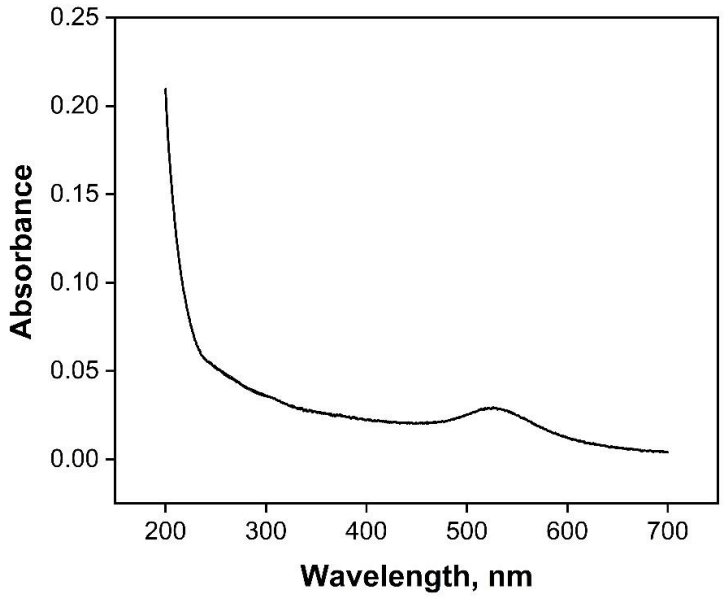


Figure 1. Spectrophotometric response of AuNP (0.1 M PBS, [AuNP]: 0.61 mM)

The use of nanomaterials in the colorimetric analysis allows the determination of the target analyte at low concentrations. The spectrophotometric response of piperacillin and tazobactam in the presence of AuNPs is shown in Figure 2. According to the figure, tazobactam and piperacillin absorption values were observed to increase in the presence of AuNP (Figure 2A and Figure 2B). The improvement of the absorption values of AuNPs indicates that it will be a suitable nanomaterial for the determination of tazobactam and piperacillin in colorimetric sensor design.

http://dx.doi.org/10.29228/jrp.399
J Res Pharm 2023; 27(3): 1066-1075

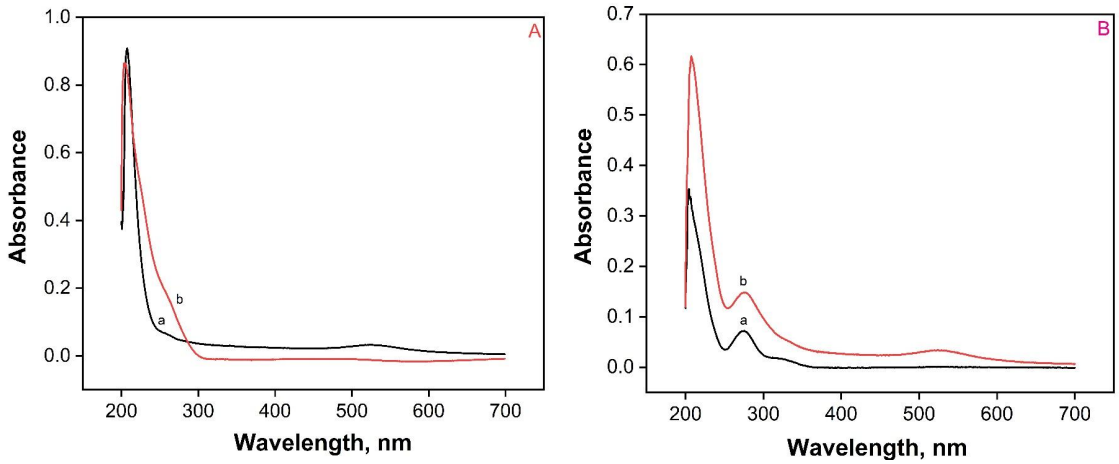
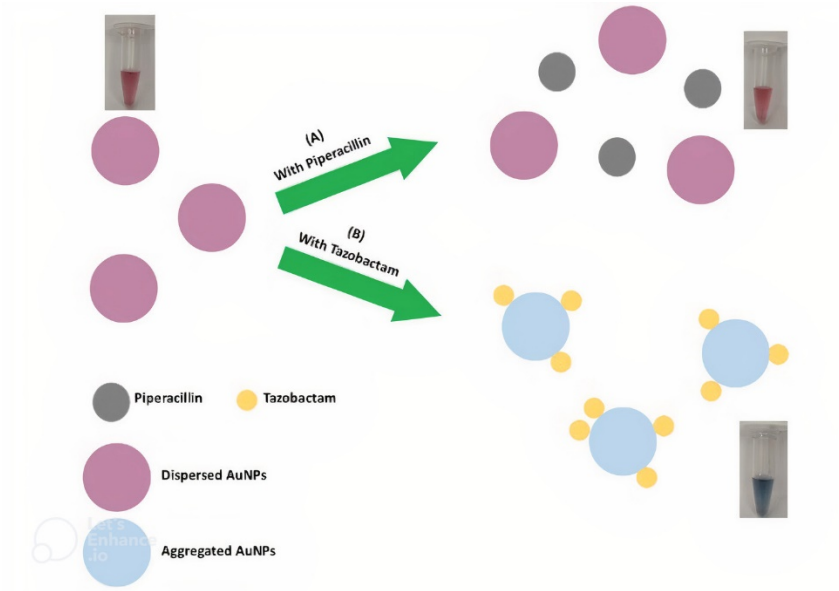


Figure 2. A) UV spectrum of a) Piperacillin and b) piperacillin-AuNPs, B) UV spectrum of a) Tazobactam and b) tazobactam-AuNPs (0.1 M PBS, [AuNPs]: 0.61 mM , [Pip]: 25.83 mg/L, [Tazo]: 15.01 mg/L)

The mechanism of the colorimetric sensing of tazobactam and piperacillin is shown in Scheme 1. In colorimetric methods based on plasmonic nanoparticles, the detection mechanism proceeds through the aggregation or non-aggregation of the nanoparticle. In the colorimetric method developed using AuNP within the scope of this study, the detection mechanism of tazobactam proceeds through AuNP aggregation, while the detection mechanism of piperacillin proceeds through non-aggregation.



Scheme 1. The sensing mechanism of proposed colorimetric detection

DLS can be helpful in determining the mechanisms of nanoparticle-based colorimetric methods because it provides information about the change in nanoparticle sizes. Whereas an unaggregated AuNPs will have a hydrodynamic size that is similar to TEM size of a nanoparticle, an aggregated AuNPs will have a hydrodynamic size that is larger than TEM size of a nanoparticle [27]. After the added of piperacillin, the hydrodynamic size of the AuNPs was not changed (Figure 3C). After the addition of tazobactam, the hydrodynamic size of AuNP raised from 21.06 nm to 675.77 nm, indicating AuNPs aggregation (Figure 3A-3B).

http://dx.doi.org/10.29228/jrp.399
J Res Pharm 2023; 27(3): 1066-1075

Journal of Research in Pharmacy
Research Article

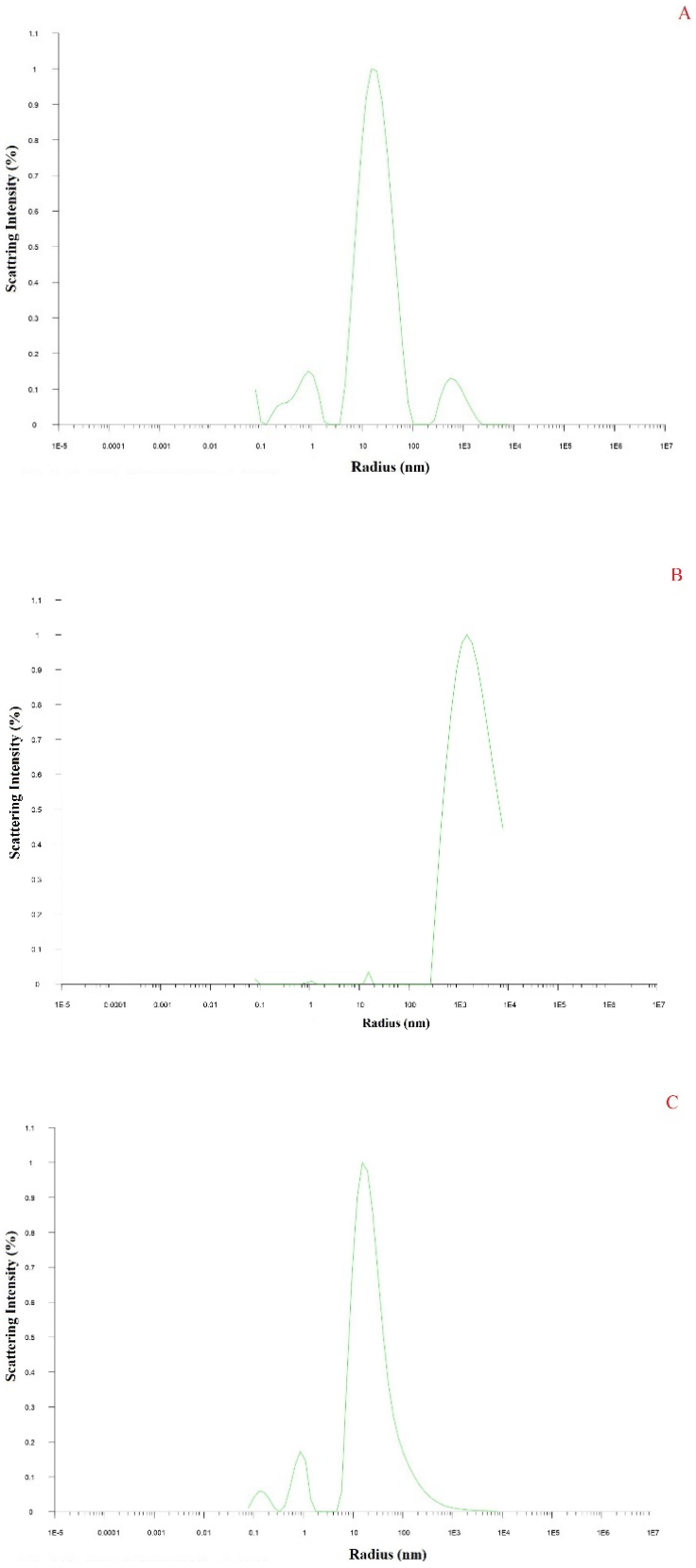


Figure 3. Measurements of DLS A)AuNPs, B)tazobactam-AuNPs and C) piperacillin-AuNPs

http://dx.doi.org/10.29228/jrp.399
J Res Pharm 2023; 27(3): 1066-1075

Optimizing ambient conditions is very important to develop an accurate, sensitive and reliable analysis method. For the developed colorimetric sensor, the effect of ambient pH and AuNPs amount on the absorption value was investigated. The change in absorbance values was examined by changing the AuNPs concentration to 0.61 mM (100 μL), 1.22 mM (200 μL), 1.83 mM (300 μL), 2.45 mM (400 μL) and 3.05 mM (500 μL) at constant tazobactam and piperacillin concentrations. It was observed that the maximum absorbance ratio was obtained when 0.61 mM (100 μL) AuNPs were used, and the absorbance ratio value decreased when the AuNPs value was increased (Figure 4a). When the amount of nanoparticles increased, the absorbance values of tazobactam and piperacillin were expected to improve and the absorbance ratio increased, while the absorbance ratio value decreased with the increase of the nanoparticle amount. It was thought that the reason for this was that the increased amount of AuNPs caused a decrease in the absorption response of tazobactam and piperacillin by acting as an interference effect, rather than improving it. For further studies, 0.61 mM (100 µL) AuNPs, which has the maximum absorbance ratio, was chosen as the optimum amount. The pH value of the working environment is very effective in colorimetric analyzes based on nanomaterials. For the colorimetric analysis of tazobactam and piperacillin, the effect of ambient pH on the absorbance ratio was investigated by changing the pH values between 7.0-11.0 at constant tazobactam and piperacillin concentrations. Since the best absorbance value for tazobactam was obtained at pH 9.0 and pH 9.5 for piperacillin (Figure 4b), the optimum pH was chosen as 9.0 for tazobactam and 9.5 for piperacillin.

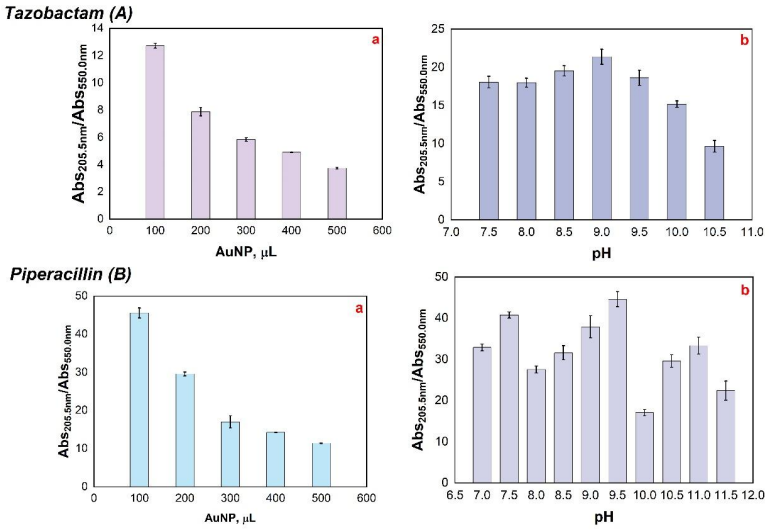


Figure 4. Optimization of experimental parameters a) AuNPs amount, b) pH (0.1 M PBS, [AuNPs]:61.0 µM, [Pip]: 25.83 mg/L, [Tazo]: 15.01 mg/L)

The linear working range of the colorimetric sensor developed for the determination of tazobactam and piperacillin was determined by calculating the absorbance ratios (Abstazo/AbsAuNPs and Abspip/AbsAuNPs) by measuring the absorbance values of tazobactam and piperacillin at different concentrations in the presence of a fixed concentration of AuNPs. Tazobactam showed a linear response with a limit of detection (LOD) of 1.01 mg/L in the concentration range of 2.25-30.04 mg/L (Figure 5).

Piperacillin showed a linear response with a detection limit of 0.29 mg/L (LOD) in the concentration range of 0.52-10.33 mg/L (LOD=3.3xsb/m, sb: standard deviation of 8 different measurements taken with the lowest concentration in the calibration graph, m: slope of the calibration graph) (Figure 6). The LOD value obtained using the developed colorimetric sensor is lower than the studies previously published in the literature [28, 29].

http://dx.doi.org/10.29228/jrp.399
J Res Pharm 2023; 27(3): 1066-1075

Journal of Research in Pharmacy
Research Article

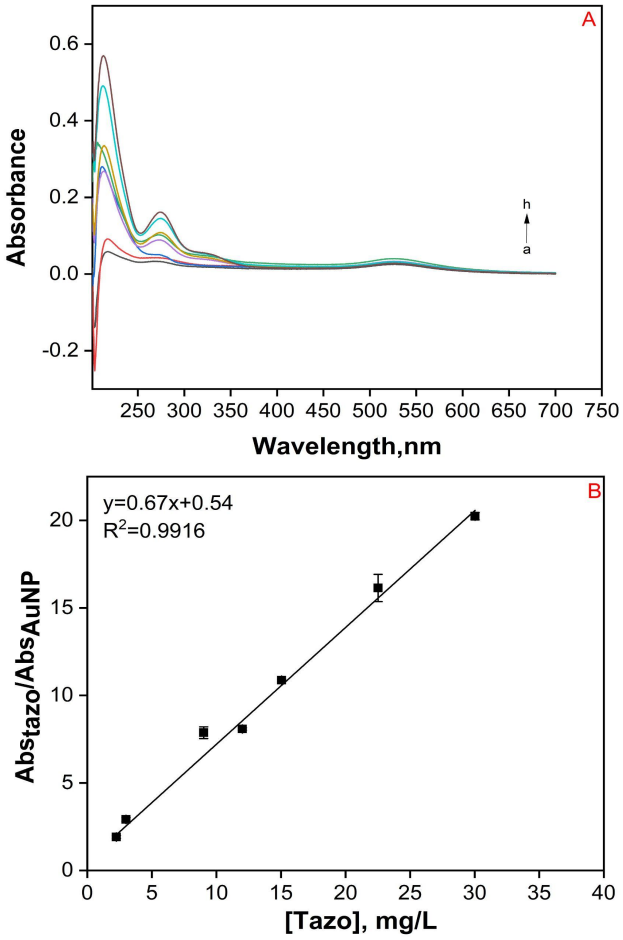
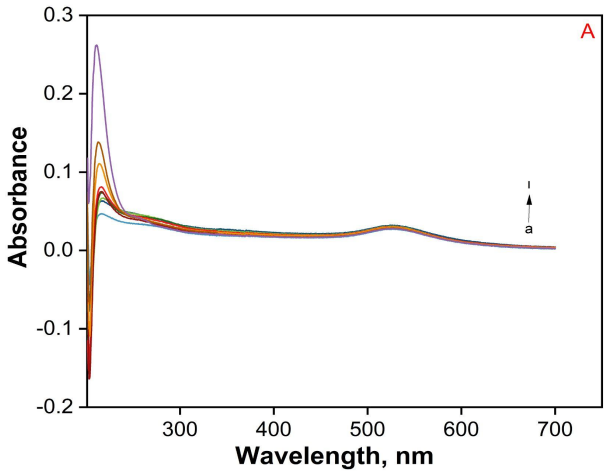


Figure 5. A) Spectrophotometric response for tazobactam B) Calibration graph for tazobactam (100 mM PBS pH 9.0, [AuNPs]: 61.0 µM, a-h: 2.25-30.04 mg/L)



http://dx.doi.org/10.29228/jrp.399
J Res Pharm 2023; 27(3): 1066-1075

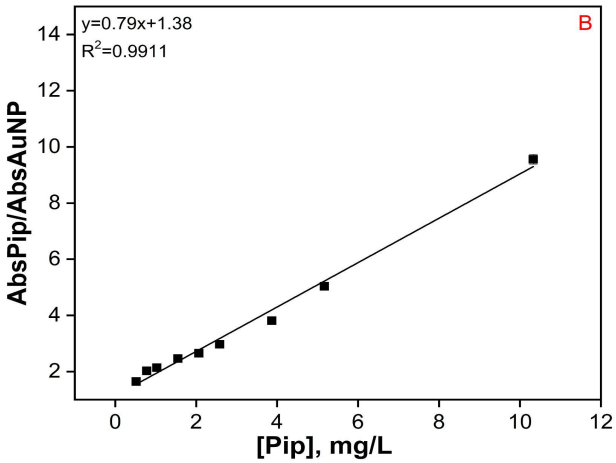


Figure 6. A) Spectrophotometric response for piperacillin B) Calibration graph for piperacillin (100 mM PBS pH 9.5, [AuNPs]: 61.0 µM, a-h: 0.52-10.33 mg/L)

The accuracy and precision of the developed nanoparticle based spectrophotometric method were assessed in terms of RE and RSD%, respectively. The RE (%) for both Tazo and Pip were found in the range of -5.66-2.66 for intra-day and-4.33- -0.19 for inter-day (Table 1). For tazobactam and piperacillin, the intra-day and intra-day precisions (RSD%) were 1.53-4.87% and 0.68-5.42%, respectively. All the results obtained show that the accuracy and precision of the developed method is quite good.

Table 1. Results of accuracy and precision of intraday and interday

Intraday Analysis									
Tazobactam					**Piperacillin**				
Amount Added (mg/L)	***Amount Found (mg/L)***	***%Recovery***	***%RSD***	***%RE***	***Amount Added (mg/L)***	***Amount Found (mg/L)***	***%Recovery***	***%RSD***	***%RE***
6.00	5.87±0.09	97.72±1.54	1.53	-2.17	5.17	4.88±0.21	94.41±4.12	4.30	-5.60
9.01	9.25±0.23	102.67±2.58	2.55	2.66	10.33	10.36±0.48	100.3±4.63	4.63	0.29
Interday Analysis									
Tazobactam					**Piperacillin**				
Amount Added (mg/L)	***Amount Found (mg/L)***	***%Recovery***	***%RSD***	***%RE***	***Amount Added (mg/L)***	***Amount Found (mg/L)***	***%Recovery***	***%RSD***	***%RE***
6.00	5.87±0.13	97.89±2.31	2.21	-2.62	5.17	4.98±0.27	96.39±5.23	5.42	-3.68
9.01	8.62±0.42	95.77±4.65	4.87	-4.33	10.33	10.31±0.07	99.80±0.75	0.68	-0.19

The performance evaluation of the colorimetric method developed using AuNPs was performed by comparing the results obtained for the determination of tazobactam and piperacillin with various methods reported in the literature. The results in Table 2 show that the developed colorimetric method is better and/or comparable to other reported methods.

http://dx.doi.org/10.29228/jrp.399
J Res Pharm 2023; 27(3): 1066-1075

Table 2. Comparison of the performance characteristics of several methods reported in the literature with the developed AuNPs-based colorimetric method

Method	Substrate	Linear Working Range (mg/L)	LOD (mg/L)	Ref.
Spectrophotometry	Tazobactam	3.00-18.00	2.79	[30]
LC-MS/MS	Piperacillin	1.00-45.00	-	[31]
HPLC-UV	Piperacillin	1.00-100.00	0.05	[32]
	Tazobactam	1.00-100.00	0.13	
Derivative Spectrophotometry	Piperacillin	10.33-51.69	0.17	[33]
	Tazobactam	3.00-15.02	0.29	
Capillary Zone Electrophoresis	Piperacillin	20.00-40.00	0.96	[34]
	Tazobactam	10.00-100.00	0.56	
RP-HPLC	Piperacillin	0.78-50.00	0.40	[28]
	Tazobactam	1.00-200.00	0.20	
Colorimetry	Tazobactam	2.25-30.04	1.01	This work
	Piperacillin	0.52-10.33	0.29	

3. CONCLUSION

In present study, we have designed a new colorimetric method using AuNPs for tazobactam and piperacillin analysis. AuNPs, known as plasmonic nanoparticles, have allowed to detection of tazobactam and piperacillin in low concentrations through their resonance absorbance bands. The proposed method has exhibited a wide working range (2.25-30.04 mg/L for tazobactam, 0.52-10.33mg/L for piperacillin) and a low detection limit. The linear equations for tazobactam and piperacillin were Absratio= 0.67[Tazo]+0.54 (R^2=0.9916) and Absratio = 0.79[Pip]+1.38 (R^2 = 0.9911), respectively. It is considered that the proposed colorimetric method based on AuNPs can be used in the clinical analysis because of exhibited good performance.

4. MATERIALS AND METHODS

4.1. Chemicals and devices

Piperacillin, tazobactam, gold nanoparticle (AuNP, 14 nm), NaH_2PO_4 and Na_2HPO_4 were purchased from Sigma-Aldrich (St. Louis, MO, USA). Other chemicals used in the experimental studies were obtained from Sigma-Aldrich (St. Louis, MO, USA), Merck (Darmstadt, Germany) and Tekkim (Istanbul, Turkey). Colorimetric analyzes were performed with the RAYLEIGH UV 1601 UV-Vis spectrophotometer (Beijing, China). The pH values of the solutions were measured using the Ohaus Starter 2100 pH meter and the combined pH electrode. The aqueous solutions used in the experimental studies were prepared daily with

http://dx.doi.org/10.29228/jrp.399
J Res Pharm 2023; 27(3): 1066-1075

distilled water obtained from the Microtest purification system. Measurements of Dynamic Light Scattering (DLS) were taken from Middle East Technical University Central Laboratory (Ankara, Turkey).

4.2. Colorimetric detection process

Standard solutions of tazobactam and piperacillin (10 mM) prepared by dissolving with distilled water were diluted with 0.1 M phosphate buffer solution (PBS) to obtain solutions at different concentrations. Standard AuNP (1200 ppm) solution was also diluted 1:10 with 0.1 M phosphate buffer solution. The mixture solutions prepared using AuNP, piperacillin and tazobactam solutions were taken into a quartz cuvette and UV absorption spectrum were recorded in the wavelength range of 200.0-700.0 nm. Tazobactam determination was performed using $AbsTazo_{208.0nm}/AbsAuNP_{526.0nm}$ absorbance ratio, and piperacillin determination was performed using $AbsPip_{205.5nm}/AbsAuNP_{526.0nm}$ absorbance ratio. All colorimetric measurements were taken in triplicate at room temperature.

Acknowledgements: This study was supported by the Coordinatorship of Scientific Research Projects of Yuksek Ihtisas University with a project number BAP no: 2020/03.001

Author contributions: Concept – H.B., Z.O.E.; Design – Z.O.E., H.B; Supervision – Z.O.E., H.B.; Resources – Z.O.E., H.B.; Materials – H.B., Z.O.E.; Data Collection and/or Processing – Z.O.E., H.B.; Analysis and/or Interpretation – Z.O.E., H.B.; Literature Search – H.B., Z.O.E., Writing – Z.O.E., H.B.; Critical Reviews – H.B., Z.O.E.

Conflict of interest statement The authors declared no conflict of interest.

REFERENCES

[1] Nanda V, Koder RL. Designing artificial enzymes by intuition and computation. Nat Chem. 2010; 2:15-24. https://doi.org/10.1038/nchem.473
[2] Raynal M, Ballester P, Vidal-Ferran A, van Leeuwen PWNM. Supramolecular catalysis. Part 2: artificial enzyme mimics. Chem Soc Rev. 2014; 43: 1734-1787. https://doi.org/10.1039/c3cs60037h
[3] Dong Z, Luo Q, Liu J. Artificial enzymes based on supramolecular scaffolds. Chem Soc Rev. 2012; 41:7890-7908. https://doi.org/10.1039/c2cs35207a
[4] Kelly KL, Coronado E, Zhao LL, Schatz GC. The optical properties of metal nanoparticles: the influence of size, shape, and dielectric environment. J Phys Chem B. 2003; 107: 668. https://doi.org/10.1021/jp026731y
[5] Ray PC. Size and shape dependent second order nonlinear optical properties of nanomaterials and their application in biological and chemical sensing. Chem Rev. 2010; 110: 5332-5365. https://doi.org/10.1021/cr900335q
[6] Yin T, Qin W. Applications of nanomaterials in potentiometric sensors. TrAc Trends Anal Chem. 2013; 51: 79-86. https://doi.org/10.1016/j.trac.2013.06.009
[7] Xu N, Jin S, Wang L. Metal nanoparticles-based nanoplatforms for colorimetric sensing: A review. Rev Anal Chem. 2021; 40: 1-11. https://doi.org/10.1515/revac-2021-0122
[8] Sau TK, Rogach AL, Jäckel F, Klar TA, Feldmann J. Properties and applications of colloidal nonspherical noble metal nanoparticles. Adv Mater. 2010; 22: 1805-1825. https://doi.org/10.1002/adma.200902557
[9] Song Y, Wei W, Qu X. Colorimetric biosensing using smart materials. Adv Mater. 2011; 23: 4215–4236. https://doi.org/10.1002/adma.201101853
[10] Peng HI, Miller BL. Recent advancements in optical DNA biosensors: exploiting the plasmonic effects of metal nanoparticles. Analyst. 2011; 136: 436-447. https://doi.org/10.1039/c0an00636j
[11] Motl NE, Smith AF, DeSantis CJ, Skrabalak SE. Engineering plasmonic metal colloids through composition and structural design. Chem Soc Rev. 2014; 43 (11): 3823-3834. https://doi.org/10.1039/c3cs60347d
[12] Sharma A, Shrivas K, Tapadia K, Ghosale A. Application of nanoparticles as a chemical sensor for analysis of enviromental samples, Chapter 13. Green Sustainable process for Chemical and Enviromental Engineering and Science, Analytical Techniques for Enviromental and Industrial Analysis. 2021; p.257. https://doi.org/10.1016/B978-0-12-821883-9.00010-2
[13] El-Sayed IH, Huang XH, El-Sayed MA. Surface plasmon resonance scattering and absorption of anti-EGFR antibody conjugated gold nanoparticles in cancer diagnostics: Applications in oral cancer. Nano Lett. 2005; 5: 829-834. https://doi.org/10.1021/nl050074e
[14] Safina G. Application of surface plasmon resonance for the detection of carbohydrates, glycoconjugates, and measurement of the carbohydrate-specific interactions: A comparison with conventional analytical techniques. A critical review. Anal Chim Acta. 2012; 712: 9-29. https://doi.org/10.1016/j.aca.2011.11.016
[15] Law WC, Yong KT, Baev A, Hu R, Prasad PN. Nanoparticle enhanced surface plasmon resonance biosensing: Application of gold nanorods. Opt Express. 2009; 17: 19041-19046. https://doi.org/10.1364/OE.17.019041

[16] Boozer C, Kim G, Cong S, Guan HW, Londergan T. Looking towards label-free biomolecular interaction analysis in a high-throughput format: a review of new surface plasmon resonance technologies. Curr Opin Biotechnol. 2006; 17: 400-405. https://doi.org/10.1016/j.copbio.2006.06.012
[17] Lu X, Zheng H, Li WQ, Yuan XX, Li H, Deng LG, Zhang H, Wang WZ, Yang GS, Meng M, Xi RM, Aboul-Enein HY. Detection of ractopamine residues in pork by surface plasmon resonance based biosensor inhibition immunoassay. Food Chem. 2012; 130: 1061-1065. https://doi.org/10.1016/j.foodchem.2011.07.133
[18] Li Y, Liu X, Lin Z. Recent developments and applications of surface plasmon resonance biosensors for the detection of mycotoxins in foodstuffs. Food Chem. 2012; 132: 1549-1554. https://doi.org/10.1016/j.foodchem.2011.10.109
[19] Kreno LE, Hupp JT, Van Duyne RP. 2010. Metal−organic framework thin film for enhanced localized surface plasmon resonance gas sensing. Anal Chem. 2010; 82: 8042-8046. https://doi.org/10.1021/ac102127p
[20] Qiao LF, Wang D, Zuo LJ, Ye YQ, Qian J, Chen HZ, He SL. Localized surface plasmon resonance enhanced organic solar cell with gold nanospheres. Appl Energy. 2011; 88: 848-885. https://doi.org/10.1016/j.apenergy.2010.09.021
[21] Kim J, Choi H, Nahm C, Park B. Surface-plasmon resonance for photoluminescence and solar-cell applications. Electron Matter. 2012; 8: 351-364. https://doi.org/10.1007/s13391-012-2117-8
[22] Bryson HM, Brogden RE. Piperacillin/tazobactam: a review of its antibacterial activity, pharmacokinetic properties and therapeutic potential. Drugs. 1994; 47(3): 506- 535. https://doi.org/10.2165/00003495-199447030-00008
[23] Rice LB, Carias LL, Shlaes DM. In vivo efficacies of β-lactam- β-lactamase inhibitor combinations against a TEM26-producing strain of Klebsiella pneumoniae. Antimicrob Agents Chemother. 1994; 38: 2663-2664. https://doi.org/10.1128/aac.38.11.2663
[24] Thauvin-Eliopoulos C, Tripodi MF, Moellering RC Jr, Eliopoulos GM. Efficacies of piperacillin-tazobactam and cefepime in rats with experimental intra-abdominal abscesses due to an extended-spectrum β lactamase-producing strain of Klebsiella pneumoniae. Antimicrob Agents Chemother. 1997; 41: 1053-1057. https://doi.org/10.1128/aac.41.5.1053
[25] Fournier JL, Ramisse F, Jacolot AC, Szatanik M, Petitjean OJ, Alonso JM, Scavizzi MR. Assessment of two penicillins plus β-lactamase inhibitors versus cefotaxime in treatment of murine Klebsiella pneumoniae infections. Antimicrob Agents Chemother. 1996; 40: 325-30. https://doi.org/10.1128/aac.40.2.325
[26] Perry CM, Markham A. Piperacillin/Tazobactam: An updated review of its use in the treatment of bacterial infections. Drugs. 1999; 57 (5): 805-843. https://doi.org/10.2165/00003495-199957050-00017
[27] Titus D, Samuel EJJ, Roopan SM. Nanoparticle characterization techniques. In: Green synthesis, characterization and applications of nanoparticles, Elsevier, 2019, pp. 303-319. https://doi.org/10.1016/B978-0-08-102579-6.00012-5
[28] Veillette JJ, Winans SA, Forland SC, Maskiewicz VK. A simple and rapid RP-HPLC method for the simultaneous determination of piperacillin and tazobactam in human plasma. J Phar Biomed Anal. 2016; 131: 80-86. https://doi.org/10.1016/j.jpba.2016.08.010
[29] Sangeetha S, Arul B, Alexandar S, Jaykar B. Development and validation of UV spectrophotometric area under curve method for quantitative estimation of piperacillin and tazobactam. Int J Chemtech Res. 2017; 10(2): 988-994.
[30] Kant R, Bodla R, Bhutani R, Kapoor G, Goswami S. Spectrophotometric absorbance correction method for the estimation of Tazobactam and Cefepime in combined tablet dosage forms. J Chem Pharm Res. 2015; 7.6: 648-656.
[31] Ferrari D, Ripa M, Premaschi S, Banfi G, Castagna A, Locatelli M. LC-MS/MS method for simultaneous determination of linezolid, meropenem, piperacillin and teicoplanin in human plasma samples. J Pharm Biomed Anal. 2019; 169: 11-18. https://doi.org/10.1016/j.jpba.2019.02.037
[32] Milla P, Ferrari F, Muntoni E, Sartori M, Ronco C, Arpicco S. Validation of a simple and economic HPLC-UV method for the simultaneous determination of vancomycin, meropenem, piperacillin and tazobactam in plasma samples. J Chromatogr B. 2020; 1148: 122151. https://doi.org/10.1016/j.jchromb.2020.122151
[33] Toral MI, Nova-Ramirez F, Nacaratte F. Simultaneous determination of piperacillin and tazobactam in the pharmaceutical formulation Tazonam® by derivative spectrophotometry. J Chilean Chem Soc. 2012; 57(2): 1189-1193. http://doi.org/10.4067/S0717-97072012000200028
[34] Al-Attas A, Nasr JJ, El-Enany N, Belal F. A green capillary zone electrophoresis method for the simultaneous determination of piperacillin, tazobactam and cefepime in pharmaceutical formulations and human plasma. Biomed Chromatogr. 2015; 29(12): 1811-1818. https://doi.org/10.1002/bmc.3500