Tolerance and Resistance of Carbapenemase Producing Klebsiella Oxytoca Against Amoxyclav, Ceftazidime and Penicillin

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**Abstract:**Carbapenemase-producing *Klebsiella oxytoca* (CP-KO) presents a significant clinical challenge due to its resistance to multiple antibiotic classes and strong biofilm-forming ability. This study evaluated the tolerance and resistance of CP-KO to commonly used antibiotics amoxicillin-clavulanate, penicillin, and ceftazidime both individually and in combination. Biochemical characterization confirmed typical *K. oxytoca*, including positive indole, VP, citrate, and urease activity. Cell viability assays showed that *K. oxytoca* lysates reduced *E. coli* cells. Crystal violet and microscopic biofilm assays shows that monotherapy yielded limited biofilm inhibition, while combination treatments particularly amoxicillin with ceftazidime resulted in significant biomass reduction.

**Keywords:** *Klebsiella oxytoca*; Carbapenemase; Biofilm inhibition; Antibiotic combination therapy

# Introduction

*Klebsiella species* are opportunistic Gram-negative pathogens frequently associated with healthcare-associated infections such as *pneumonia*, urinary tract infections, and septicemia [(Asokan et al., 2025)](https://paperpile.com/c/yEJ3Wn/fEAma). The rise of carbapenemase-producing *Klebsiella* strains poses a serious public health threat due to their broad resistance to multiple antibiotic classes, particularly β-lactams and carbapenems. Among them carbapenemase-producing *Klebsiella oxytoca* (CP-KO) has emerged as a significant concern in healthcare settings [(Wan et al., 2023)](https://paperpile.com/c/yEJ3Wn/kIMa3). These organisms produce enzymes that hydrolyze carbapenems, rendering them resistant to this important class of antibiotics. Identified carbapenemases in *K. oxytoca*, including KPC, VIM, OXA-48, and NDM [(Pérez-Vazquez et al., 2019)](https://paperpile.com/c/yEJ3Wn/IH0uD). Recent research has revealed that *K. oxytoca* is a complex of nine species, including *K. grimontii, K. huaxiensis,* and *K. michiganensis*n [(Yang et al., 2022)](https://paperpile.com/c/yEJ3Wn/dTnaZ). This taxonomic complexity adds a layer of challenge to the study and management of carbapenemase-producing strains within the *K. oxytoca* complex[(Ajay et al., 2023; Chokkattu et al., 2023; Padarthi et al., 2023)](https://paperpile.com/c/yEJ3Wn/8RVL3+WBFYl+Q7U3Z). The emergence of CP-KO poses a significant threat to public health due to its ability to acquire antimicrobial resistance genes and carry multiple virulence factors [(Ikhimiukor et al., 2023)](https://paperpile.com/c/yEJ3Wn/14y3g). The blaKPC-2 gene is the most common carbapenemase gene found in the *K. oxytoca* complex, primarily located on IncN or IncF plasmids [(Lerminiaux et al., 2023)](https://paperpile.com/c/yEJ3Wn/KnYVe). These resistant strains has been observed in various environmental niches, including hospitals, wastewater treatment plants, and rivers, highlighting the potential for widespread dissemination [(Ebomah & Okoh, 2020)](https://paperpile.com/c/yEJ3Wn/lm970). The tolerance and resistance of CPKO against amoxicillin-clavulanate, ceftazidime, and penicillin are of particular concern[(Dharman et al., 2023; S. Sindhu et al., 2023; Sreenivasagan et al., 2023)](https://paperpile.com/c/yEJ3Wn/O6JDv+lRJfq+itO6Z) . Studies have shown high resistance rates to these antibiotics among *Klebsiella species*. A study by [(Dwomoh et al., 2022)](https://paperpile.com/c/yEJ3Wn/PVjd6)found that 75% of multidrug-resistant *E. coli* and *K. pneumoniae* isolates were resistant to amoxicillin-clavulanate, and 64.6% were resistant to ceftazidime.Amoxicillin-clavulanate, ceftazidime, and penicillin are antibiotics commonly used to treat bacterial infections. However, their effectiveness against K. pneumoniae varies. Ceftazidime, a third-generation cephalosporin, has shown broad-spectrum activity against Enterobacteriaceae, including Klebsiella species [(Aziz et al., 2019)](https://paperpile.com/c/yEJ3Wn/QC6Az). The emergence of ceftazidime-avibactam (CZA) resistance in *Klebsiella species* has been reported, primarily due to mutations in the KPC enzymes[(Ramakrishnan et al., 2023; Shenoy & Maiti, 2023; J. S. Sindhu et al., 2023)](https://paperpile.com/c/yEJ3Wn/XHXbd+tQZWa+38F8s). These mutations not only confer resistance to CZA but also impact susceptibility to other β-lactam antibiotics, including ceftazidime and piperacillin-tazobactam [(Findlay et al., 2021)](https://paperpile.com/c/yEJ3Wn/oKk2N). The prevalence of extended-spectrum β-lactamase (ESBL) production in *Klebsiella species* further complicates the treatment landscape. A study found that 45% of Klebsiella isolates were ESBL producers, with K. pneumoniae showing a higher prevalence (50%) compared to K. oxytoca (25%) [(Al-Sheboul et al., 2023)](https://paperpile.com/c/yEJ3Wn/ru9ka).While resistance enables bacteria to grow in the presence of elevated drug concentrations, tolerance and persistence allow bacterial populations to survive prolonged exposure to lethal antibiotic doses. These mechanisms are significant barriers to successful treatment, often resulting in infection relapse and increased chances for resistance evolution during therapy [(Sidders et al., 2022; Sulaiman & Lam, 2022)](https://paperpile.com/c/yEJ3Wn/9YJOI+puGiW). Notably, studies have shown that tolerance often precedes the development of resistance. For example, in Pseudomonas aeruginosa, intermediate drug tolerance emerged first, followed by divergent evolutionary paths leading to high-level tolerance or antibiotic resistance [(Santi et al., 2021)](https://paperpile.com/c/yEJ3Wn/rrNQm). This study aims to evaluate the tolerance and resistance of carbapenemase-producing *Klebsiella oxytoca* (CPKO) to antibiotics.

# Material and methods

*Klebsiella oxytoca* samples were collected from hospitals and the bacteria were cultured on MacConkey agar and incubated for 24 hours at 37°C. Following incubation, the colonial morphology of *klebsiella oxytoca* was examined under a microscope. A biochemical analysis was performed using samples obtained from, where the pathogen was streaked on MacConkey agar for identification. Various biochemical characteristics were evaluated in accordance with the guidelines outlined in [(Buchanan & Gibbons, 1974)](https://paperpile.com/c/yEJ3Wn/7yoYn). Specifically, the tests conducted included indole production, the methyl red test, the Voges-Proskauer test, citrate utilization, lactose fermentation, catalase activity, urease activity, inositol fermentation, and triple sugar iron agar, as well as maltose, sucrose, xylose, and starch tests. The cell viability of Carbapenemase producing *Klebsiella oxytoca* on non-clinical bacterial cells was evaluated by the method proposed by [(Alenazy, 2023)](https://paperpile.com/c/yEJ3Wn/NcRbp) with cell lysate. Bacterial culture (500µL) was centrifuged at 10000 rpm for 5 minutes and the cells were suspended in 0.85% saline. Various concentrations (250-1000 𝜇g/ml) of added into the bacterial suspension and incubate for 5 minutes, then add 1µL of PI dye in 100µL of bacterial suspension to mix well and incubate in 15 minutes. After incubation equal volume of PBS was added and the optical density was measured at 540 nm. DAPI stained cultures in room temperature (37°C) are used as positive control. The percentage of viable cells are calculated using a given formula.

Viability (%) = [(Control−test sample)/test] x100.

The crystal violet (CV) assay was used to determine the adherent viable cell biomass after antibiotic treatment. Overnight bacterial cultures were adjusted to an OD600 of 0.1, and 200 µL was inoculated into 96-well microtiter plates. After incubation at 37°C for 24 hours, non-adherent cells were removed, and wells were washed three times with PBS. Adherent cells were fixed with ethanol for 10 minutes, stained with 0.1% (w/v) crystal violet for 15 minutes, and rinsed thoroughly with distilled water. After air-drying, the bound dye was solubilized using 200 µL of 95% ethanol, and absorbance was measured at 570 nm using a microplate reader. All tests were performed in triplicate [(O’Toole, 2011)](https://paperpile.com/c/yEJ3Wn/LwyXi).Biofilm formation was allowed to proceed for 48 hours, after which the biofilm was gently rinsed twice with phosphate-buffered saline (pH 7.4) to remove any planktonic cells. The biofilm was subsequently treated with 1000 mg/ml of various antibiotics, including amoxiclav, penicillin, ceftazidime, a combination of penicillin and ceftazidime, a combination of amoxiclav and ceftazidime, and a combination of amoxiclav and penicillin, for 24 hours. Following the incubation period, the biofilm was fixed with 70% ethanol for 15 minutes and stained with 100 μl of acridine orange. The stained slides were then observed under a light microscope to evaluate biofilm inhibition.

# Results

*Klebsiella oxytoca* is a Gram-negative, non-motile, rod-shaped bacterium that does not produce spores but is encapsulated, which significantly enhances its pathogenicity by protecting the organism from host immune responses(Nikalje et al., 2024) (Chehelgerdi et al., 2023).In the current study, *K. oxytoca's* biochemical characterisation showed a catalase-positive and oxidase-negative profile, indicating that it can detoxify reactive oxygen species without having cytochrome c oxidase activity.The isolate produced indole, indicating enzymatic breakdown of tryptophan, and showed a positive Voges-Proskauer (VP) reaction, showing acetoin synthesis via glucose fermentation. Citrate utilisation was also positive, showing that the organism could utilise citrate as its only carbon source, which is a characteristic that enteric bacteria frequently exhibit. *K. oxytoca* differs from other Enterobacteriaceae species that produce hydrogen sulphide (H2S). Positive Triple Sugar Iron (TSI) and gas generation test results showed that the organism fermented glucose with the creation of gas and acid.Through the MUG assay, it tested positive for β-glucuronidase but did not show any gelatinase activity. Its metabolic flexibility was further demonstrated by the bacterium's positive nitrate reduction and urease activity results (Table 1).Carbohydrate fermentation tests revealed that *K. oxytoca* could metabolise a range of sugars, including arabinose, cellobiose, glucose, glycerol, inositol, lactose, maltose, mannitol, mannose, raffinose, rhamnose, starch, sorbitol, and xylose. Sucrose fermentation was negative, and there was no DNase activity. This wide-ranging fermentation characteristics of carbohydrates highlights the organism's ecological adaptation and metabolic diversity (Table 2). Enzymatic activity  showed positive  for lysine decarboxylase and phenylalanine deaminase, indicating that the bacteria has capacity to decarboxylate lysine and deaminate phenylalanine, biomarkers useful in differentiating *K. oxytoca* from other Enterobacteriaceae species. However, the activities of lipase, tryptophan deaminase, and tyrosine hydrolysis were negative (Table 3).A cell viability analyse shows the cytotoxic effect of *Klebsiella oxytoca* cell lysate on *Escherichia coli* (Fig.1). The cell count of the control group, which was not exposed to lysate, was 10¹² CFU/mL. Treatment with increasing concentration of *K. oxytoca* lysate (250, 500, 750, and 1000 µg/mL) shows decreasing viable *E. coli* cells. At 250 µg/mL, the count reduced to 10⁹ CFU/mL, a 3-log reduction. Treatment at 500 µg/mL resulted in a 10⁷ CFU/mL count. Compared to the untreated control cells decreased to 10⁶ CFU/mL at 750 µg/mL and then to a significant decline to 10⁴ CFU/mL at the the maximum concentration of 1000 µg/mL.The results of this study show that *Klebsiella oxytoca* has a strong biofilm-forming ability under untreated conditions, as shown by a high biomass value of 97% measured by the crystal violet assay (Fig. 2). Monotherapy with separate antibiotics showed little antibiofilm effectiveness. Penicillin and amoxiclave specifically decreased the biomass of biofilms to 78% and 83%. In comparison, Cefatazidime showed higher antibiofilm action, reducing biomass by 63%. The use of combination antibiotics  resulted in significantly greater antibiofilm effects. The combination of Penicillin and Cefatazidime reduced biofilm biomass to 40%. Combinations of Amoxiclave and Cefatazidime and Amoxiclave and Penicillin showed the most significant decreases, reducing the biomass to 21% and 23%, respectively. A biofilm is a complex aggregation of microorganisms, embedded in a self-produced matrix of extracellular polymeric substances, enabling them to adhere to surfaces and resist environmental stresses, including antibiotic treatments. In this study, the antibiofilm efficacy of individual antibiotics and their combinations against *Klebsiella oxytoca* was evaluated at a concentration of 1000 𝜇g/ml, using an untreated biofilm as the control (Fig. 3a). The control sample exhibited a dense and well-structured biofilm, typical of *Klebsiella oxytoca* growth under untreated conditions. Treatment with amoxiclav resulted in moderate antibiofilm activity, with noticeable thinning of the biofilm matrix. Although some areas of the biofilm exhibited partial disruption, large portions remained intact, suggesting that amoxiclav reduced the biofilm's density but was not potent enough to cause complete biofilm disintegration (Fig. 3b). Treatment with Penicillin demonstrated stronger antibiofilm activity compared to amoxiclav. The biofilm treated with penicillin showed visible thinning and less dense structural organization. Penicillin was more effective than amoxiclav (Fig. 3c). Ceftazidime exhibited the most substantial antibiofilm activity among the individual antibiotics, causing extensive disruption of the biofilm matrix. Large regions of the biofilm were disintegrated, leading to a notable reduction in the overall biofilm mass. This indicated that ceftazidime had a stronger ability to break down the biofilm structure compared to both amoxiclav and penicillin (Fig. 3d). The combination of penicillin and ceftazidime showed enhanced antibiofilm activity, with significant disruption of the biofilm structure and an extensive reduction in biofilm density (Fig. 3e). The synergistic interaction between these two antibiotics resulted in a more efficient breakdown of the biofilm compared to the effects of the antibiotics used individually. The combination of amoxiclav and ceftazidime exhibited the most potent antibiofilm activity (Fig. 3f). This combination nearly eradicated the biofilm, leaving only minimal traces, and demonstrated a strong synergistic effect that surpassed the efficacy of any other treatment . Finally, the combination of amoxiclav and penicillin also showed significant antibiofilm activity, although it was slightly less effective than the amoxiclav-ceftazidime combination (Fig. 3g). The biofilm treated with this combination showed considerable thinning and fragmentation, with a substantial reduction in biofilm coverage, though more biofilm remained compared to the amoxiclav-ceftazidime treatment.

# Discussion

This study shows *Klebsiella oxytoca's* potent biofilm-forming ability, which is consistent with its recognised role in chronic infections and antibiotic resistance [(Yang et al., 2022)](https://paperpile.com/c/yEJ3Wn/dTnaZ). Monotherapy with penicillin and amoxyclav had minimal antibiofilm effects, indicating poor penetration and β-lactamase-mediated resistance [(Karaiskos et al., 2022)](https://paperpile.com/c/yEJ3Wn/4acaQ). Ceftazidime was more effective (63%), confirming its overall activity against Gram-negative bacteria [(Findlay et al., 2021)](https://paperpile.com/c/yEJ3Wn/oKk2N)[(Kasabwala et al., 2021; Rajeshkumar & Lakshmi, 2021; Varghese et al., 2023)](https://paperpile.com/c/yEJ3Wn/3dwzX+1ENE7+06hsa). Combination of antibiotics reduces the biomass due to improved β-lactamase inhibition and deeper biofilm penetration [(Satapoomin et al., 2022)](https://paperpile.com/c/yEJ3Wn/2uqVt).*K. oxytoca* produces cytotoxins such as tilivalline and tilimycin, which can disrupt DNA and cellular processes [(Unterhauser et al., 2019)](https://paperpile.com/c/yEJ3Wn/XucxM)[(Keerthana & Ramesh, 2021; Murugesan, 2021; Tiwari & Jain, 2021)](https://paperpile.com/c/yEJ3Wn/366Hw+lBlNX+ChiSE)[(Keerthana & Ramesh, 2021; Murugesan, 2021; Subramanian et al., 2021; Tiwari & Jain, 2021)](https://paperpile.com/c/yEJ3Wn/366Hw+lBlNX+ChiSE+ISfkr). Additionally, outer membrane vesicles (OMVs) and bacteriocins may contribute to this inhibitory effect by delivering toxic molecules or targeting closely related bacterial species [(O’Donoghue & Krachler, 2016)](https://paperpile.com/c/yEJ3Wn/mKZuZ). A study found that 97.5% of ampicillin-resistant *K. pneumoniae* isolates formed biofilms, highlighting a strong correlation between biofilm production and antibiotic resistance. Resistance rates for cephalosporins in biofilm-forming isolates ranged from 80-95%, indicating that biofilms protect bacteria from these antibiotics [(Darwiesh et al., 2024)](https://paperpile.com/c/yEJ3Wn/WZEj3). Ceftazidime, particularly in combination with avibactam, has shown promise against carbapenem-resistant *K. pneumoniae*[*(Evaluation Composite Restoration Posterior Teeth Proanthocyanidin Pretreatment Liner Using Fédération Dentaire Internationale Criteria: Split-Mouth Randomized Controlled Trial, n.d.; Pranati et al., 2021; Sakthi & Department of Public Health Dentistry, 2021)*](https://paperpile.com/c/yEJ3Wn/Bq3MD+2saSV+80WjB)[*(G. & Ganapathy, 2022; Kumar & Ramesh, 2021)*](https://paperpile.com/c/yEJ3Wn/E43qi+RiOdy)). The combination restores ceftazidime's efficacy by inhibiting β-lactamases [(Wu et al., 2024)](https://paperpile.com/c/yEJ3Wn/5rHEG). However, high concentrations of avibactam are necessary to maintain ceftazidime's activity against resistant strains [(Palombo et al., 2023)](https://paperpile.com/c/yEJ3Wn/IeqMz). The presence of biofilms necessitates the use of combination therapies to enhance the effectiveness of antibiotics like ceftazidime and potentially amoxiclav, which may also benefit from similar strategies [(Geng et al., 2024)](https://paperpile.com/c/yEJ3Wn/cjrQT).

# Conclusion

The study confirms that *Klebsiella oxytoca* exhibits strong biofilm formation and antibiotic tolerance, complicating treatment strategies. While single antibiotics showed limited antibiofilm efficacy, combination therapies, especially amoxicillin-clavulanate with ceftazidime, demonstrated strong inhibition of biofilm biomass and structure. These findings highlight the significance of using synergistic antibiotic combinations in clinical settings to efficiently target CP-KO biofilms and reduce resistance-associated treatment failures.

# References

1. [Ajay, R., JafarAbdulla, M. U., Sivakumar, J. S., Baburajan, K., Rakshagan, V., & Eyeswarya, J. (2023). Dental alloy adhesive primers and bond strength at alloy-resin interface: A systematic review and meta-analyses. The Journal of Contemporary Dental Practice, 24(8), 521–544.](http://paperpile.com/b/yEJ3Wn/WBFYl)
2. [Alenazy, R. (2023). Antimicrobial Activities and Biofilm Inhibition Properties of Trigonella foenumgraecum Methanol Extracts against Multidrug-Resistant Staphylococcus aureus and Escherichia coli. Life (Basel, Switzerland), 13(3). https://doi.org/](http://paperpile.com/b/yEJ3Wn/NcRbp)[10.3390/life13030703](http://dx.doi.org/10.3390/life13030703)
3. [Al-Sheboul, S. A., Al-Madi, G. S., Brown, B., & Hayajneh, W. A. (2023). Prevalence of extended-spectrum β-lactamases in multidrug-resistant Klebsiella pneumoniae isolates in Jordanian hospitals. Journal of Epidemiology and Global Health, 13(2), 180–190.](http://paperpile.com/b/yEJ3Wn/ru9ka)
4. [Asokan, S., Jacob, T., Jacob, J., AlSosowaa, A. A., Cherian, T., Peijnenburg, W. J. G. M., & Vijayan, S. (2025). Klebsiella pneumoniae: A growing threat in the era of antimicrobial resistance. The Microbe, 7(100333), 100333.](http://paperpile.com/b/yEJ3Wn/fEAma)
5. [Aziz, S. N., Al-Sallami, K. J., Abd, S. Y., A., A.-M. A. M., Mohammed, M. A., H., A. A. M., & Mohammed, S. Q. (2019). Improving the antibacterial activity by the combination of zirconium oxide nanoparticles (ZrO2) and ceftazidime against Klebsiella pneumoniae. Global Journal of Public Health Medicine, 1(1), 16–20.](http://paperpile.com/b/yEJ3Wn/QC6Az)
6. [Buchanan, R. E., & Gibbons, N. E. (1974). Bergey’s manual of determinative bacteriology. cabidigitallibrary.org.](http://paperpile.com/b/yEJ3Wn/7yoYn)
7. Chehelgerdi M., Chehelgerdi, M., Allela, O. Q. B., Pecho, R. D. C., Jayasankar, N., Rao, D. P. & Akhavan-Sigari, R. (2023). Progressing nanotechnology to improve targeted cancer treatment: overcoming hurdles in its clinical implementation. Molecular cancer, 22(1), 169.
8. [Chokkattu, J. J., Mary, D. J., Shanmugam, R., & Neeharika, S. (2023). Evaluation clove ginger-mediated titanium oxide nanoparticles-based dental varnish against Streptococcus mutans Lactobacillus Species: vitro study. World J Dent, 14(3), 233–237.](http://paperpile.com/b/yEJ3Wn/Q7U3Z)
9. [Darwiesh, S. M. M., Al-Shamahy, H. A., El-Aghbary, D. A., Al-Moyed, K. A., AL-Mabashi, A. A., & Al-Shawkany, A. M. (2024). The association between antibiotic resistance and biofilm production in Klebsiella pneumoniae isolated from urinary tract infections. مجلة جامعة صنعاء للطب والعلوم الصحية, 18(2), 13–20.](http://paperpile.com/b/yEJ3Wn/WZEj3)
10. [Dharman, S., Maragathavalli, G., Shanmugam, R., & Shanmugasundaram, K. (2023). Curcumin mediated gold nanoparticles analysis its antioxidant, anti-inflammatory, antimicrobial activity against oral pathogens. Pesquisa Brasileira Em Odontopediatria E Clínica Integrada, 23.](http://paperpile.com/b/yEJ3Wn/lRJfq)
11. [Dwomoh, F. P., Kotey, F. C. N., Dayie, N. T. K. D., Osei, M.-M., Amoa-Owusu, F., Bannah, V., Alzahrani, F. M., Halawani, I. F., Alzahrani, K. J., Egyir, B., & Donkor, E. S. (2022). Phenotypic and genotypic detection of carbapenemase-producing Escherichia coli and Klebsiella pneumoniae in Accra, Ghana. PloS One, 17(12), e0279715.](http://paperpile.com/b/yEJ3Wn/PVjd6)
12. [Ebomah, K. E., & Okoh, A. I. (2020). Detection of carbapenem-resistance genes in Klebsiella species recovered from selected environmental niches in the Eastern Cape Province, South Africa. Antibiotics (Basel, Switzerland), 9(7), 425.](http://paperpile.com/b/yEJ3Wn/lm970)
13. [Evaluation Composite Restoration Posterior Teeth Proanthocyanidin Pretreatment Liner Using Fédération Dentaire Internationale Criteria: Split-mouth Randomized Controlled Trial. (n.d.).](http://paperpile.com/b/yEJ3Wn/80WjB)
14. [Findlay, J., Poirel, L., Juhas, M., & Nordmann, P. (2021). KPC-Mediated Resistance to Ceftazidime-Avibactam and Collateral Effects in Klebsiella pneumoniae. Antimicrobial Agents and Chemotherapy, 65(9), e0089021.](http://paperpile.com/b/yEJ3Wn/oKk2N)
15. [Geng, X., Yang, Y.-J., Li, Z., Ge, W.-B., Xu, X., Liu, X.-W., & Li, J.-Y. (2024). Fingolimod inhibits exopolysaccharide production and regulates relevant genes to eliminate the biofilm of K. pneumoniae. International Journal of Molecular Sciences, 25(3), 1397.](http://paperpile.com/b/yEJ3Wn/cjrQT)
16. [G., K. E. V., & Ganapathy, D. (2022). Operator errors in failed composite restoration-A review. Int J Dent Oral Sci, 8(7), 2941–2944.](http://paperpile.com/b/yEJ3Wn/RiOdy)
17. [Ikhimiukor, O. O., Souza, S. S. R., Akintayo, I. J., Marcovici, M. M., Workman, A., Martin, I. W., & Andam, C. P. (2023). Phylogenetic lineages and antimicrobial resistance determinants of clinical Klebsiella oxytoca spanning local to global scales. Microbiology Spectrum, e0054923.](http://paperpile.com/b/yEJ3Wn/14y3g)
18. [Karaiskos, I., Galani, I., Papoutsaki, V., Galani, L., & Giamarellou, H. (2022). Carbapenemase producing Klebsiella pneumoniae: implication on future therapeutic strategies. Expert Review of Anti-Infective Therapy, 20(1), 53–69.](http://paperpile.com/b/yEJ3Wn/4acaQ)
19. [Kasabwala, H., Nallaswamy, D., Subhashree, R., & Ahmed, N. (2021). Evaluation Of Overall Marginal Accuracy Of DMLS Copings Fabricated Using 3 Different DMLS Printing Machines. Int J Dentistry Oral Sci, 8(7), 3335–3340.](http://paperpile.com/b/yEJ3Wn/1ENE7)
20. [Keerthana, T., & Ramesh, S. (2021). Knowledge, attitude and practice survey on awareness of the association between diet and dental erosion. International Journal of Dentistry and Oral Science, 8(2), 1533–1540.](http://paperpile.com/b/yEJ3Wn/lBlNX)
21. [Kumar, I. L., & Ramesh, S. (2021). Knowledge, Attitude and Practices (KAP) survey of shade selection for indirect veneers. Int J Dent Oral Sci, 26, 2856–2864.](http://paperpile.com/b/yEJ3Wn/E43qi)
22. [Lerminiaux, N., Mitchell, R., Bartoszko, J., Davis, I., Ellis, C., Fakharuddin, K., Hota, S. S., Katz, K., Kibsey, P., Leis, J. A., Longtin, Y., McGeer, A., Minion, J., Mulvey, M., Musto, S., Rajda, E., Smith, S. W., Srigley, J. A., Suh, K. N., … Canadian Nosocomial Infection Surveillance Program. (2023). Plasmid genomic epidemiology of blaKPC carbapenemase-producing Enterobacterales in Canada, 2010-2021. Antimicrobial Agents and Chemotherapy, 67(12), e0086023.](http://paperpile.com/b/yEJ3Wn/KnYVe)
23. [Murugesan, A. (2021). Saravana Dinesh SP evaluation of shear bond strength of ceramic brackets with two different base designs: An in-vitro study. Int J Dentistry Oral Sci.](http://paperpile.com/b/yEJ3Wn/ChiSE) <https://www.academia.edu/download/72981941/IJDOS_2377_8075_08_304.pdf>
24. Nikalje, A. V., Tajane, S. T., Kocharekar, A., Vekariya, D., & Patil, H. (2024, April). Detecting Cancer through Analysis of Histopathological Images. In 2024 International Conference on Expert Clouds and Applications (ICOECA) (pp. 579-585). IEEE.
25. [O’Donoghue, E. J., & Krachler, A. M. (2016). Mechanisms of outer membrane vesicle entry into host cells. Cellular Microbiology, 18(11), 1508–1517.](http://paperpile.com/b/yEJ3Wn/mKZuZ)
26. [O’Toole, G. A. (2011). Microtiter dish biofilm formation assay. Journal of Visualized Experiments: JoVE, 47. https://doi.org/](http://paperpile.com/b/yEJ3Wn/LwyXi)[10.3791/2437](http://dx.doi.org/10.3791/2437)
27. [Padarthi, L. C., Anumula, L., Chinni, S. K., Sannapureddy, S., & Govula, K. (2023). Evaluation Composite Restoration Posterior Teeth Proanthocyanidin Pretreatment Liner Using Fédération Dentaire Internationale Criteria: Split-mouth Randomized Controlled Trial. International Journal Prosthodontics Restorative Dentistry, 13(4), 191–200.](http://paperpile.com/b/yEJ3Wn/8RVL3)
28. [Palombo, M., Secci, B., Bovo, F., Gatti, M., Ambretti, S., & Gaibani, P. (2023). In vitro evaluation of increasing avibactam concentrations on ceftazidime activity against ceftazidime/avibactam-susceptible and resistant KPC-producing Klebsiella pneumoniae clinical isolates. Antibiotics (Basel, Switzerland), 12(12). https://doi.org/](http://paperpile.com/b/yEJ3Wn/IeqMz)[10.3390/antibiotics12121707](http://dx.doi.org/10.3390/antibiotics12121707)
29. [Pérez-Vazquez, M., Oteo-Iglesias, J., Sola-Campoy, P. J., Carrizo-Manzoni, H., Bautista, V., Lara, N., Aracil, B., Alhambra, A., Martínez-Martínez, L., Campos, J., & Spanish Antibiotic Resistance Surveillance Program Collaborating Group. (2019). Characterization of carbapenemase-producing Klebsiella oxytoca in Spain, 2016-2017. Antimicrobial Agents and Chemotherapy, 63(6). https://doi.org/](http://paperpile.com/b/yEJ3Wn/IH0uD)[10.1128/AAC.02529-18](http://dx.doi.org/10.1128/AAC.02529-18)
30. [Pranati, T., Ranjan, M., & Sandeep, A. H. (2021). Marginal adaptability custom made cast post made different techniques-a literature review. Int J Dentistry Oral Sci, 8(8), 3954–3959.](http://paperpile.com/b/yEJ3Wn/Bq3MD)
31. [Rajeshkumar, S., & Lakshmi, T. (2021). Biomedical potential of zinc oxide nanoparticles synthesized using plant extracts. Int J Dent Oral Sci, 8, 4160–4163.](http://paperpile.com/b/yEJ3Wn/06hsa)
32. [Ramakrishnan, M., Shanmugam, R., Neeharika, S., Chokkattu, J. J., Thangavelu, L., & Khanna, N. (2023). Anti-inflammatory activity and cytotoxic effect of ginger and Rosemary-mediated titanium oxide nanoparticles-based dental varnish. World Journal of Dentistry, 14(9), 761–765.](http://paperpile.com/b/yEJ3Wn/tQZWa)
33. [Sakthi, S., & Department of Public Health Dentistry,(2021). Thymus vulgaris mediated selenium nanoparticles, characterization and its antimicrobial activity - an in vitro study. International Journal of Dentistry and Oral Science, 3516–3521.](http://paperpile.com/b/yEJ3Wn/2saSV)
34. [Santi, I., Manfredi, P., Maffei, E., Egli, A., & Jenal, U. (2021). Evolution of antibiotic tolerance shapes resistance development in chronic Pseudomonas aeruginosa infections. mBio, 12(1). https://doi.org/](http://paperpile.com/b/yEJ3Wn/rrNQm)[10.1128/mBio.03482-20](http://dx.doi.org/10.1128/mBio.03482-20)
35. [Satapoomin, N., Dulyayangkul, P., & Avison, M. B. (2022). Klebsiella pneumoniae mutants resistant to ceftazidime-avibactam plus aztreonam, imipenem-relebactam, meropenem-vaborbactam, and cefepime-taniborbactam. Antimicrobial Agents and Chemotherapy, 66(4), e0217921.](http://paperpile.com/b/yEJ3Wn/2uqVt)
36. [Shenoy, N. D., & Maiti, S. (2023). Evaluation marginal fit CAD/CAM crowns using CBCT digital scanners. Annals Dental Specialty, 11(3-2023), 37–44.](http://paperpile.com/b/yEJ3Wn/XHXbd)
37. [Sidders, A. E., Kedziora, K. M., Beam, J. E., Bui, D. T., Parsons, J. B., Rowe, S. E., & Conlon, B. P. (2022). Antibiotic-induced accumulation of lipid II sensitizes bacteria to antimicrobial fatty acids. In bioRxiv. https://doi.org/](http://paperpile.com/b/yEJ3Wn/puGiW)[10.1101/2022.05.03.490474](http://dx.doi.org/10.1101/2022.05.03.490474)
38. [Sindhu, J. S., Maiti, S., & Nallaswamy, D. (2023). Comparative analysis on efficiency and accuracy of parallel confocal microscopy and three-dimensional in motion video with triangulation technology-based intraoral scanner under influence of moisture and mouth opening - A crossover clinical trial. Journal of Indian Prosthodontic Society, 23(3), 234–243.](http://paperpile.com/b/yEJ3Wn/38F8s)
39. [Sindhu, S., Maiti, S., & Nallaswamy, D. (2023). Factors affecting accuracy intraoral scanners-a systematic review. Annals Dental Specialty, 11(1-2023), 40–52.](http://paperpile.com/b/yEJ3Wn/O6JDv)
40. [Sreenivasagan, S., Subramanian, A. K., Mohanraj, K. G., & Kumar, R. S. (2023). Assessment of toxicity of Green Synthesized Silver Nanoparticle-coated Titanium Mini-implants with Uncoated Mini-implants: Comparison in an Animal Model Study. The Journal of Contemporary Dental Practice, 24(12), 944–950.](http://paperpile.com/b/yEJ3Wn/itO6Z)
41. [Subramanian, E., Ravindran, V., & Jeevanandan, G. (2021). Comparison of amount of tooth reduction in primary first molar for stainless steel, zirconia and fibre-glass crowns–in-vitro study. International Journal of Dentistry and Oral Science, 8(7), 3427–3430.](http://paperpile.com/b/yEJ3Wn/ISfkr)
42. [Sulaiman, J. E., & Lam, H. (2022). Proteomics in antibiotic resistance and tolerance research: Mapping the resistome and the tolerome of bacterial pathogens. Proteomics, 22(8), e2100409.](http://paperpile.com/b/yEJ3Wn/9YJOI)
43. [Tiwari, A., & Jain, R. K. (2021). The effect of motivational and reminder therapy on the compliance of patients wearing fixed appliances. Int J Dent Oral Sci, 8(7), 3303–3305.](http://paperpile.com/b/yEJ3Wn/366Hw)
44. [Unterhauser, K., Pöltl, L., Schneditz, G., Kienesberger, S., Glabonjat, R. A., Kitsera, M., Pletz, J., Josa-Prado, F., Dornisch, E., Lembacher-Fadum, C., Roier, S., Gorkiewicz, G., Lucena, D., Barasoain, I., Kroutil, W., Wiedner, M., Loizou, J. I., Breinbauer, R., Díaz, J. F., … Zechner, E. L. (2019). Klebsiella oxytoca enterotoxins tilimycin and tilivalline have distinct host DNA-damaging and microtubule-stabilizing activities. Proceedings of the National Academy of Sciences of the United States of America, 116(9), 3774–3783.](http://paperpile.com/b/yEJ3Wn/XucxM)
45. [Varghese, R., Maliael, M., & Subramanian, A. (2023). Antibacterial activity of nanoparticle-coated orthodontic archwires: A systematic review. Journal of International Oral Health: JIOH, 15(1), 1.](http://paperpile.com/b/yEJ3Wn/3dwzX)
46. [Wan, W., Yang, X., Yu, H., Wang, M., Jia, W., Huang, B., Qu, F., Shan, B., Tang, Y.-W., Chen, L., & Du, H. (2023). Genomic characterization of carbapenem-resistant Klebsiella oxytoca complex in China: a multi-center study. Frontiers in Microbiology, 14, 1153781.](http://paperpile.com/b/yEJ3Wn/kIMa3)
47. [Wu, Y., Yu, W., Chu, X., Zhang, J., Jia, P., Liu, X., Zhu, Y., Xu, Y., & Yang, Q. (2024). Effect of ceftazidime-avibactam combined with different antimicrobials against carbapenem-resistant Klebsiella pneumoniae. Microbiology Spectrum, 12(6), e0010724.](http://paperpile.com/b/yEJ3Wn/5rHEG)
48. [Yang, J., Long, H., Hu, Y., Feng, Y., McNally, A., & Zong, Z. (2022). Klebsiella oxytoca complex: Update on taxonomy, antimicrobial resistance, and virulence. Clinical Microbiology Reviews, 35(1), e0000621.](http://paperpile.com/b/yEJ3Wn/dTnaZ)