THE NEW ARMENIAN MEDICAL JOURNAL
Volume18 (2024), Issue 1 p. 98-105

DOI: https://doi.org/10.56936/18290825-18.2024-98

REPURPOSING PAROXETINE: INVESTIGATION OF ANTIBACTERIAL AND ANTI-ADHESIVE PROPERTIES OF THE ANTI-DEPRESSION DRUG AGAINST MAJOR PATHOGENS CAUSING CATHETER-ASSOCIATED URINARY TRACT INFECTIONS

Tahane B.M.A., Poyil M.M.*

Department of Basic Medical Sciences, College of Medicine, Prince Sattam bin Abdulaziz University, Al-Kharj, Saudi Arabia.

Received 16.12.2023, Accepted for printing 15.12.2023

Abstract

Objective: *Catheter-associated urinary tract infections make one of the leading nosocomial diseases worldwide. Most of the bacteria causing catheter-associated urinary tract infections form protective biofilms inside which the pathogens would be more resistant to antimicrobial agents, making the treatment more complicated resulting in severe sufferings of the patients with prolonged morbidity, increased hospital expenses and comparatively higher mortality. Treatment of infections caused by two of such pathogens - Enterococcus faecalis and Escherichia coli are challenging and the pharmaceutical world is trying to find alternative antimicrobial agents. Thus, the current investigation is a trial to repurpose paroxetine - an anti-depression drug to evaluate its antibacterial potentials against these pathogens.*

Material and methods *The repurposing of paroxetine to evaluate its efficiency against Enterococcus faecalis and Escherichia coli was performed by agar diffusion method. Using microdilution protocols, the minimal inhibitory concentration was also calculated. To qualitatively analyse the anti-biofilm activity of the drug, paroxetine was coated on catheters and the activity was evaluated against the bacterial growth.*

Results: *Paroxetine exhibited promising antibacterial activity and the minimum inhibitory concentrations were found to be 75 µg/ml and 37.5 µg/ml against Enterococcus faecalis and Escherichia coli respectively. The drug could also reduce the formation of biofilms by 72% in the case of Enterococcus faecalis and by 86% in case of Escherichia coli. Paroxetine also shown to possess potential anti-adhesive properties.*

Conclusion**:** *The results suggest that the anti-depression drug paroxetine has antibacterial, anti-biofilm and anti-adhesive properties against two of the most prevalent bacteria involved in catheter-associated urinary tract infections*

Keywords: *Anti-biofilm, anti-depression, minimum inhibitory concentrations, paroxetine, repurposing.*

Cite This Article as:

Tahane .M.A, Poyil M.M. (2024). Repurposing paroxetine: investigation of Antibacterial and anti-Adhesive properties of the anti-depression drug against major pathogens causing catheter-associated urinary tract infections; The New Armenian Medical Journal, vol.18(1), 98-105; DOI: https://doi.org/10.56936/18290825-18.2024-98

Address for Correspondence:

Muhammad Musthafa Poyil, PhD
Department of Basic Medical Sciences, College of Medicine, Prince Sattam bin Abdulaziz University
Al-Kharj-11942, Saudi Arabia
Tel.: +966565634412
E-mail: m.poyil@psau.edu.sa

Introduction

Urinary system plays an important role in excreting the liquid wastes from the human body. Generally, the urinary system does not allow any bacterial entry from the outer skin to bladder but sometimes the bacteria may be able to enter the system when the immune system fails resulting the occurrence of urinary tract infections (UTIs) which initiate the use of catheters [*Feneley et al., 2015*]. One of the most important indwelling medical devices is catheter which become an essential part in modern medicine for helping the hospitalized patients to improve their quality of life [*Andersen et al., 2020*; *Trautner 2010*]. Still, the infection of the catheters is occurred whether short or long term because it has more suitable environment for microbial contamination leading severe catheter-associated urinary tract infection (CAUTI) which related to more than 40% of hospital acquired infections (HAIs) [*Milo et al., 2019*]. CAUTI is a main global concern owing to high morbidity and mortality rate and ultimately, high economic burden due to extended stay in hospital, increasing healthcare maintenance, extensive chemotherapy as well as high risk for the development of antibiotic resistance [*Haque et al., 2018; Hollenbeak* and *Schilling 2018*]. The primary cause of CAUTIs has been suggested as the biofilm formation by the Gram positive as well as Gram negative bacteria on the indwelling catheter surfaces. Many reports say, *Enterococcus faecalis* and *Escherichia coli* are the prevalent microbes involved in CAUTIs [*Laupland et al., 2005; Chatterjee et al., 2014; Sievert et al., 2013*]. These prevalent organisms make the management CAUTIs very critical due to their biofilm forming ability resulting in the formation of antibiotic resistant strains. is the Biofilm, the fundamental factor for CAUTI formation is a complex dense structure attached on the catheter surfaces which produces polymeric substances to aid the bacteria to effectively avoid the antibiotic treatment rendering medical devices dysfunction [*Aleksandra et al., 2020; Di Martino 2018; Kurmoo et al., 2020*].

Since, CAUTI is mainly related to biofilm formation on catheter surfaces, there is an alarming need for researches to alternate or modify the catheter surface to avoid the biofilm formation in order to prevent further infections [*Costa et al., 2019; Junter et al., 2016*]. In other words, there is a need for the search of new anti-adhesive agents that fight against antibiotic resistance and biofilm formation of prevalent microbes involved in CAUTIs. It is in this scenario that the repurposing the drugs (used in the management of other diseases) for new application has emerged as a promising treatment choice for antibiotic resistance as they are readily available for the treatment since, the pharmacological facts are known which reduces the time, cost and risk associated with the antibiotic development [*Poyil* and *Bari, 2023*]. Thus, in the study, the antibacterial and anti-adhesive properties of paroxetine, an antidepression drug was investigated against *Enterococcus faecalis* and *Escherichia coli* prevalent microbes involved in CAUTIs.

Materials and Methods

Antibacterial activity determination: The well diffusion method was performed to investigate the antibacterial activity of the repurposing drug paroxetine against *Enterococcus faecalis* and *Escherichia coli* as described previously [*Meiyazhagan et al., 2016*]. In brief, the sterile Mueller Hinton Agar (MHA) plates were swabbed with overnight cultures of both the bacterial pathogens *viz, Enterococcus faecalis* and *Escherichia coli* followed by the addition of varying concentrations of paroxetine to each wells drilled. The plates and incubated at 37^0C for 24 to 36 hours and after the incubation plates were observed for the antibacterial activity of paroxetine by measuring the zone of inhibition around the wells in millimetres (*mm*). Ampicillin and rifampicin were used as positive controls for *Enterococcus faecalis* and *Escherichia coli* respectively. The experiment was repeated twice.

Minimum inhibitory concentrations (MICs) determination: The microdilution method was adopted to determine the paroxetine minimum inhibitory concentrations against *Enterococcus faecalis* and *Escherichia coli* [*Meiyazhagan et al., 2016*]. For the experiment, in a 96 well plate, 300 *µg/ml* of paroxetine drug was serially diluted using Mueller Hinton Broth (MHB) to obtain the final concentration as 2.3 *µg/ml*. Finally, the overnight cultures of both the bacteria were added and incubated in standard conditions. Then, the optical density of the plates was measured using spectrophotometer at 600 *nm*. The experiments were repeated thrice.

Paroxetine effect on colony formation: The effect of paroxetine on the colony formation of *Enterococcus faecalis* and *Escherichia coli* was studied as described [*Meiyazhagan et al., 2015]*. Briefly, the paroxetine drug was serially diluted using MHB in 96 well plates. The overnight cultures of mentioned bacteria were added to the well which contained various concentrations of the drug and the plates were incubated for 96 hours. Then, the phosphate buffer saline (PBS) wash was done to remove the non adherent cells followed by colony fixation using methanol. The colonies fixed were stained with 0.1% crystal violet solution. The wells were air dried after removing the excess stain. The ethanol and acetone mixture was added to dissolve the crystal violet and the obtained purple product was read at 570 *nm*. Untreated wells served as negative controls for both bacteria. The experiments were done in triplicate.

Paroxetine effect on biofilm formation: The biofilm formation assay was performed to ascertain the effect of paroxetine on biofilm formation by the bacterial pathogens *Enterococcus faecalis* and *Escherichia coli* [*Gowri et al., 2020*]. The overnight cultures of both bacteria were added in polystyrene microtiter plates and allowed for 96 hours for maturation. After that, the matured biofilm was treated for 24 hours with the paroxetine as 1X MIC and 2X MIC. Afterwards, the non adherent cells were removed by PBS wash and the attached cells were fixed with methanol for sometimes followed 0.1% crystal violet staining. The excess stain was removed and the mixture of ethanol and acetone was observed to get purple colour. The plate was measured at 570 nm. Untreated wells served as negative controls for both microbes whereas ampicillin and rifampicin treated wells served as positive controls for *Enterococcus faecalis* and *Escherichia coli* respectively. The experiment was repeated twice.

Antibacterial activity of catheter coating: The paroxetine coating catheter was evaluated for their antibacterial activity against *Enterococcus faecalis* and *Escherichia coli* using *in vitro* catheter models as per standard protocols [*Goda et al. 2022*]. In brief, the small pieces of sterile silicone catheter tube were coated with paroxetine solution for 30 mins followed by air dry. The coated catheter pieces were placed over the MHA plates which were swabbed with particular microbes and the plates were incubated in standard conditions. After incubation, the zones of inhibition around the catheter pieces were observed and considered as the proof for the antibacterial activity of paroxetine coated on catheters. Sterile catheter pieces were used as negative control.

Statistical analysis: One-way ANOVA analysis was carried out on IBM SPSS Statistics Ver. 22.0 software (SPSS Inc. in Chicago, Illinois, United States). The statistical analyses of the data from the minimum inhibitory concentrations determination, colony formation, biofilm formation assays etc. were represented as mean ± standard deviations and the statistical significance was considered, with a $p<0.05$. All the experiments were performed in triplicates.

RESULTS

Antibacterial activity determination: The determined antibacterial activity of various concentrations of paroxetine against *Enterococcus faecalis* and *Escherichia coli* is is in figure 1. The zone of inhibitions around the well which contain various concentrations indicating the antibacterial activities of paroxetine against the selected bacteria. The antibacterial activities were attained in 125 µg of paroxetine against both *Enterococcus faecalis* and *Escherichia coli*. As seen in figure, sizes of the zones of inhibition ere increased for both the microbes with respect to the increase in the paroxetine concentrations.

Minimum inhibitory concentrations determinations: The lowest concentrations of the drug paroxetine which were able to inhibit the growth of both *Enterococcus faecalis* and *Escherichia coli* were determined and the graphs were plotted as in figure 2

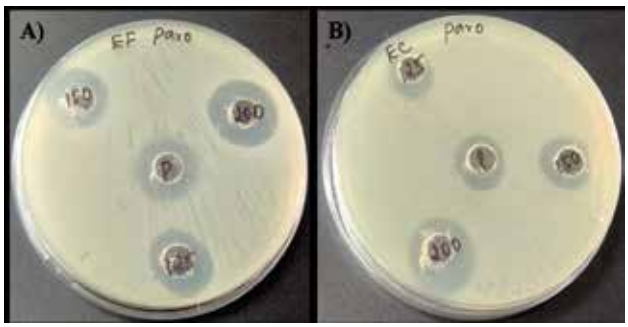

FIGURE 1. *Antibacterial activity of Paroxetine against A) Enterococcus faecalis B) Escherichia coli*

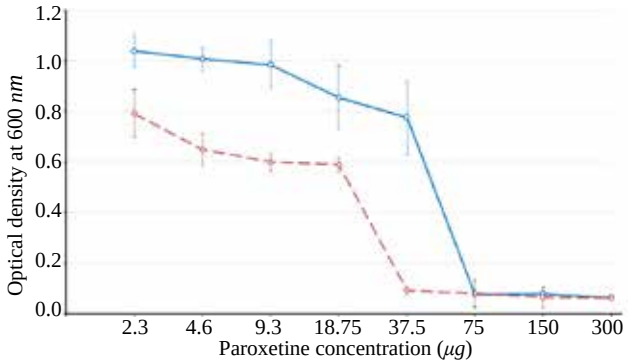

Figure 2. *Minimum inhibitory concentrations determination of paroxetine against Enterococcus faecalis (dotted line) and Escherichia coli (solid line)*

and 3. As seen in the graph, 75 *μg/ml* of paroxetine concentration was needed to inhibit the growth of *Enterococcus faecalis* whereas 37.5 *μg/ml* was enough for *Escherichia coli* growth inhibition.

Paroxetine effect on colony formation: The effect of the drug paroxetine on *Enterococcus faecalis* and *Escherichia coli* colony formation was investigated and the results are shown in figure 4 and 5. As mentioned in figure, the paroxetine was able to inhibit the colony formation of both the microbes up to its MIC level. Fortunately, the trace of paroxetine present in the well was able to decrease colony formation of *Escherichia coli* in the poly-

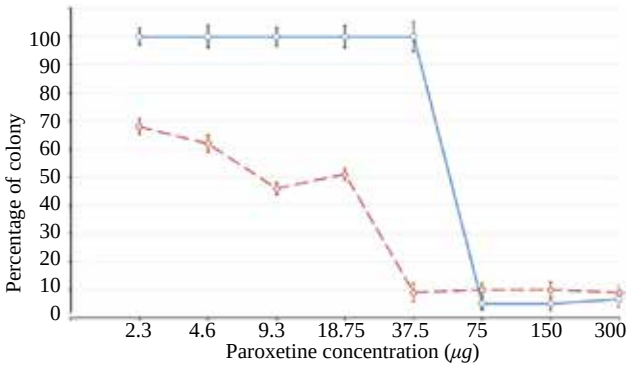

Figure 4. *Percentage of colony formation after treatment with paroxetine against Enterococcus faecalis (dotted line) and Escherichia coli (solid line)*

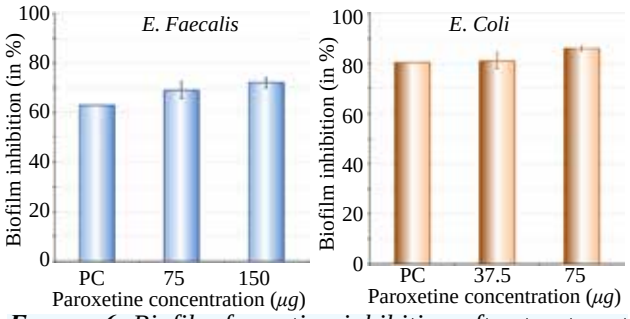

Figure 6. *Biofilm formation inhibition after treatment with paroxetine against Enterococcus faecalis and Escherichia coli. Note: PC- positive control*

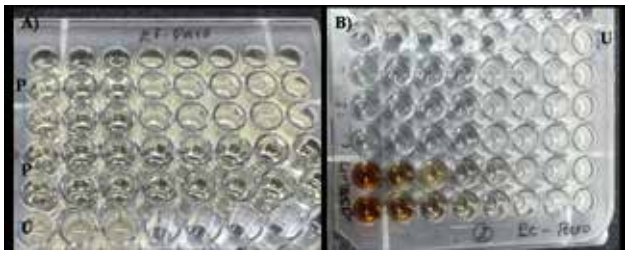

Figure 3. *Minimum inhibitory concentrations of paroxetine determination against Enterococcus faecalis (A) and Escherichia coli (B)*

styrene plate surfaces. In contrast, the *Enterococcus faecalis* colony formation was observed after the MIC level of paroxetine. This showed the efficiency of paroxetine in eliminating the colony formation of both the microbes.

Paroxetine effect on biofilm formation: The paroxetine effect on biofilm formations of *Enterococcus faecalis* and *Escherichia coli* quantified in 96 well plates are presented in figure 6 and 7. As seen in figure, the paroxetine effectively inhibited the biofilm formation of both of the bacterial pathogens, in the tested concentrations in the polystyrene surfaces. The paroxetine reduced 69% and 72% of biofilms after treatment with 1X MIC and 2X MIC respectively against *Enterococcus faecalis*. Whereas, paroxetine reduced 81% and 86% of

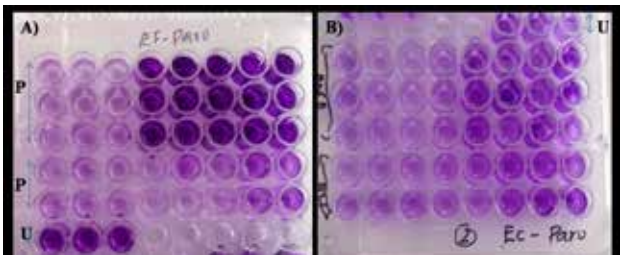

Figure 5. *Visual observation of colony formation of Enterococcus faecalis (A) and Escherichia coli (B) after treatment with paroxetine*

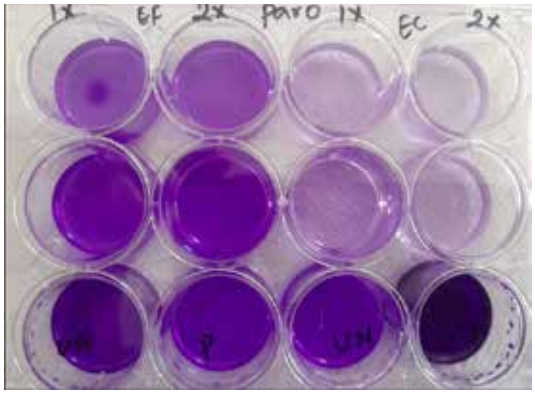

Figure 7. *Photographic view of biofilm formation after treatment with paroxetine against Enterococcus faecalis and Escherichia coli*

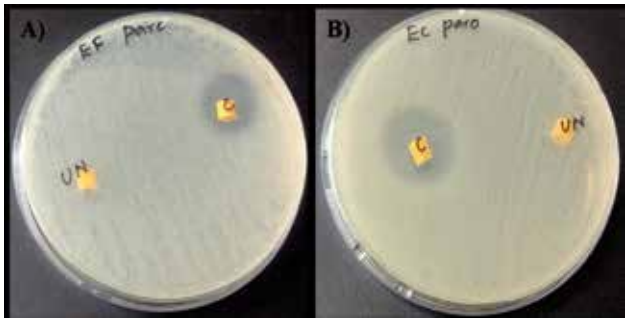

FIGURE 8. *Anti-adhesive property of paroxetine against A) Enterococcus faecalis B) Escherichia coli*

biofilm when treated with 1X MIC and 2X MIC respectively against *Escherichia coli*. It showed the ability of paroxetine in eradicating biofilms of both the selected bacteria involved in CAUTIs.

Antibacterial activity of paroxetine catheter coating: The antibacterial activity of paroxetine coated catheter is presented in figure 8. As seen in figure, the clear zone of inhibition around the paroxetine coated catheter piece indicated the anti-adhesive property of paroxetine against *Enterococcus faecalis* and *Escherichia coli*. This suggested the antibacterial and anti-adhesive property of paroxetine against prevalent organism involved in CAUTI. Whereas, the uncoated catheter piece was not showed any zone of inhibition.

DISCUSSION

The use of indwelling catheter may lead the most common CAUTIs which are related to lengthy stay in hospitals resulting high economic burden and antibiotic resistance development ultimately leading to high morbidity and mortality [*Mitchell et al., 2021; Smith et al., 2019; Fasugba et al., 2017*]. In such a situation there is an urgent call for alternative solutions for treating antibiotic resistance and for the prevention of biofilm formation on catheter surface. Therefore, in the study, the antibacterial, anti-biofilm and anti-adhesive properties of a repurposing anti-depression drug paroxetine was evaluated against *Enterococcus faecalis* and *Escherichia coli* involved in CAUTI. The paroxetine exhibited promising antibacterial activity against both bacteria - Enterococcus *faecalis* and *Escherichia coli*. Similarly, the antibacterial activity of an anti-depression drug fluoxetine was evaluated against *Pseudomonas aeruginosa*, *Escherichia coli* and *Staphylococcus aureus* and it was effectively inhibited the growth of tested microbes and also it showed elevated activity when combined with known drugs [*Karine de Sousa et al., 2018)*. Likewise, the phosphate prodrugs with anticancer activity were repurposed for their antibacterial activity against *Enterococcus faecalis* and *Staphylococcus aureus* and found have potential antibacterial activity [*Pertusati et al., 2020*]. Ebselen- the anti-inflammatory, anti-oxidant and cytoprotective drug is also known to possess antibacterial activity against vancomycin and methicillin resistant *Staphylococcus aureus* [*Thangamani et al., 2015*]. Another study by Ayaz *et al.,* 2015 showed the activity of the antidepression drug sertraline against multiple pathogenic bacteria including *Acinetobacter baumanii*, *Escherichia coli*, *Enterococcus faecalis* and *Pseudomonas aeruginosa*. Boyd et al., (2021) have showed the potential antibacterial activity of repurposed drugs such as amlodipine, azelastine, ebselen and sertraline against multidrug resistant *Staphylococcus aureus*. Many investigations have been conducted to study the antibacterial activities of repurposing drugs like duloxetine, amodiaquine, curcumin, ibuprofen, ellagic acid, diiodohydroxyquinoline, mitomycin -C and quercetin against *Psudomonas aeruginosa*, *Klebsiella pneumoniae*, *Clostridium difficile*, *Enterococcus faecalis*, *Escherichia coli*, *Staphylococcus aureus* etc. and have showed promising activities [*Ahmet, 2009; Kamurai et al., 2020; Pacios et al., 2021; Shi et al., 2022*].

Besides the antibacterial activity, the paroxetine was evaluated for their anti-biofilm activity against *Enterococcus faecalis* and *Escherichia coli* involved in CAUTIs as the CAUTI is mainly related biofilms which colonize on the catheter surface leading difficult in the management of infection [*Zhu et al., 2019*]. The biofilm starts from the attachment of microbes to any living and non-living surfaces to form matured structures which are not easily to eradicated [*Pelling et al., 2019*]. Our study showed that, in the presence of the drug paroxetine, the colony formation by the selected pathogens was not possible on the polystyrene surface which inhibited the biofilm formation in the beginning itself. Our findings are correlated with previous reports wherein the anti-biofilm and antibacterial of activities of penfluridol and etoposide –A were investigated against *Enterococcus faecalis* and *Staphylococcus aureus* [*Zeng et al., 2021; Vidhya, 2022*].

Coating of catheters with antimicrobial agents in and on the outer surface of the catheter is an excellent method to prevent the biofilm formation by the uropathogens. The drug paroxetine has also shown its anti-adhesive property as it showed against both *Enterococcus faecalis* and *Escherichia coli* when coated on catheters. Ivanova et al., (2021) have also reported a similar finding in which the catheter coated with zinc oxide nanoparticles showed potential activities against *Escherichia coli* and *Staphylococcus aureus* when treated up to seven days of [*Ivanova et al., 2021]*. Likewise, silver nanoparticle coated catheters showed excellent anti-biofilm activity against *Escherichia coli* and *Staphylococcus aureus* [*Rahuman et al., 2021*] and, fosfomycin showed activity against *Enterococcus faecalis* using bladder infectious model [*Abbott, 2020*].

Conclusion

CAUTI is an important medical problem for many people around the world and is directly related to the biofilm formation by the causative bacterial pathogens. In the present study, two of such important CAUTI causing bacteria – *viz, Enterococcus faecalis* and *Escherichia coli* were subjected to various treatments by the an antidepression drug paroxetine in an attempt to repurpose it for its antibacterial and anti-adhesive properties. The drug showed excellent capability in preventing biofilm formation on polystyrene surfaces and it also showed the activity on catheter surfaces against *Enterococcus faecalis* and *Escherichia coli*. So, the paroxetine can be further studies for using as an anti-biofilm coating material for catheters prevent biofilm formation of *Enterococcus faecalis* and *Escherichia coli*.

Acknowledgements: *The authors are grateful to the Deanship of Scientific Research, Prince Sattam bin Abdulaziz University, Al-Kharj, Saudi Arabia for its support and encouragement in conducting the research and publishing this report.*

REFERENCES

1. *Abbott, I. J., van Gorp, E., van der Meijden, A., Wijma, R. A., Meletiadis, J. ... et al., (2020).* Oral Fosfomycin Treatment for Enterococcal Urinary Tract Infections in a Dynamic *In Vitro* Model. *Antimicrobial agents and chemotherapy*, *64*(6), e00342-20. https://doi.org/10.1128/AAC.00342-20
2. *Ahmet YC, Yeliz TC, Selma KU, Belma D. (2009).* Investigation of antibacterial activity of sertralin. Mikrobiyol Bul. 2009: 651-6. https://pubmed.ncbi.nlm.nih.gov/20084919/
3. *Aleksandra I, Kristina I, Ilana P, Aharon G, Katerina T, Rositsa M, ... et al., (2020)* Layer-by-layer coating of aminocellulose and quorum quenching acylase on silver nanoparticles synergistically eradicate bacteria and their biofilms, Adv. Funct. Mater. 30 (2020) 2001284, https://doi.org/10.1002/adfm.202001284
4. *Andersen, M J., and Flores-MirelesvAL. 2020.* "Urinary Catheter Coating Modifications: The Race against Catheter-Associated Infections" Coatings 10, no. 1: 23. https://doi.org/10.3390/coatings10010023
5. *Ayaz, M., Subhan, F., Ahmed, J., Khan, A. U., Ullah, F., Ullah, I., Ali, G., Syed, N. I., & Hussain, S. (2015).* Sertraline enhances the activity of antimicrobial agents against pathogens of clinical relevance. *Journal of biological research (Thessalonike, Greece)*, *22*(1), 4. https://doi.org/10.1186/s40709-015-0028-1
6. *Boyd, N. K., Lee, G. C., Teng, C., & Frei, C. R. (2021).* In vitro activity of non-antibiotic drugs against Staphylococcus aureus clinical strains. Journal of global antimicrobial resistance, 27, 167–171. https://doi.org/10.1016/j.jgar.2021.09.003
7. *Chatterjee, S., Maiti, P., Dey, R., Kundu, A., & Dey, R. (2014).* Biofilms on indwelling urologic devices: microbes and antimicrobial management prospect. *Annals of medical and health sciences research*, *4*(1), 100–104. https://doi.org/10.4103/2141-9248.126612
8. *Costa, B., Mota, R., Parreira, P., Tamagnini, P., L Martins, M. C., & Costa, F. (2019).* Broad-Spectrum Anti-Adhesive Coating Based on an Extracellular Polymer from a Marine Cyanobacterium. *Marine drugs*, *17*(4), 243. https://doi.org/10.3390/md17040243
9. *Di Martino P. (2018).* Extracellular polymeric substances, a key element in understand-

ing biofilm phenotype. *AIMS microbiology*, *4*(2), 274–288. https://doi.org/10.3934/microbiol.2018.2.274

10. *Fasugba, O., Koerner, J., Mitchell, B. G., & Gardner, A. (2017).* Systematic review and meta-analysis of the effectiveness of antiseptic agents for meatal cleaning in the prevention of catheter-associated urinary tract infections. *The Journal of hospital infection*, *95*(3), 233–242. https://doi.org/10.1016/j.jhin.2016.10.025

11. *Feneley, R. C., Hopley, I. B., & Wells, P. N. (2015).* Urinary catheters: history, current status, adverse events and research agenda. *Journal of medical engineering & technology*, *39*(8), 459–470. https://doi.org/10.3109/03091902.2015.1085600

12. *Goda, R. M., El-Baz, A. M., Khalaf, E. M., Alharbi, N. K., Elkhooly, T. A., & Shohayeb, M. M. (2022).* Combating Bacterial Biofilm Formation in Urinary Catheter by Green Silver Nanoparticle. *Antibiotics (Basel, Switzerland)*, *11*(4), 495. https://doi.org/10.3390/antibiotics11040495

13. *Gowri, M., Jayashree, B., Jeyakanthan, J., & Girija, E. K. (2020).* Sertraline as a promising antifungal agent: inhibition of growth and biofilm of Candida auris with special focus on the mechanism of action in vitro. *Journal of applied microbiology*, *128*(2), 426–437. https://doi.org/10.1111/jam.14490

14. *Gowri, M., Sofi Beaula, W., Biswal, J., Dhamodharan, P., Saiharish, R., Rohan prasad, S., ... et al., (2016).* β-lactam substituted polycyclic fused pyrrolidine/pyrrolizidine derivatives eradicate C. albicans in an ex vivo human dentinal tubule model by inhibiting sterol 14-α demethylase and cAMP pathway. *Biochimica et biophysica acta*, *1860*(4), 636–647. https://doi.org/10.1016/j.bbagen.2015.12.020

15. *Haque, M., Sartelli, M., McKimm, J., & Abu Bakar, M. (2018).* Health care-associated infections - an overview. *Infection and drug resistance*, *11*, 2321–2333. https://doi.org/10.2147/IDR.S177247

16. *Hollenbeak, C. S., & Schilling, A. L. (2018).* The attributable cost of catheter-associated urinary tract infections in the United States: A systematic review. *American journal of infection control*, *46*(7), 751–757. https://doi.org/10.1016/j.ajic.2018.01.015

17. *Ivanova, A., Ivanova, K., Perelshtein, I., Gedanken, A., Todorova, K., Milcheva, R., ... et al., (2021).* Sonochemically engineered nano-enabled zinc oxide/amylase coatings prevent the occurrence of catheter-associated urinary tract infections. Materials science & engineering. C, Materials for biological applications, 131, 112518. https://doi.org/10.1016/j.msec.2021.112518

18. *Junter GA, Thébault P, Lebrun L. (2016).* Polysaccharide-based anti-biofilm surfaces. *Acta Biomater*. 2016;30:13-25. https://doi.org/10.1016/j.actbio.2015.11.010

19. *Kamurai, B., Mombeshora, M., & Mukanganyama, S. (2020).* Repurposing of Drugs for Antibacterial Activities on Selected ESKAPE Bacteria Staphylococcus aureus and Pseudomonas aeruginosa. International journal of microbiology, 2020, 8885338. https://doi.org/10.1155/2020/8885338

20. *Karine de Sousa, A., Rocha, J. E., Gonçalves de Souza, T., Sampaio de Freitas, T., Ribeiro-Filho, J., & Melo Coutinho, H. D. (2018).* New roles of fluoxetine in pharmacology: Antibacterial effect and modulation of antibiotic activity. *Microbial pathogenesis*, *123*, 368–371. https://doi.org/10.1016/j.micpath.2018.07.040

21. *Kurmoo, Y., Hook, A. L., Harvey, D., Dubern, J., Williams, P., Morgan, S. P., Alexander, M. R. (2020).* Real time monitoring of biofilm formation on coated medical devices for the reduction and interception of bacterial infections. Biomaterials Science, 8(5), 1464-1477. https://doi.org/10.1039/c9bm00875f

22. *Laupland, K. B., Bagshaw, S. M., Gregson, D. B., Kirkpatrick, A. W., Ross, T., & Church, D. L. (2005).* Intensive care unit-acquired urinary tract infections in a regional critical care system. *Critical care (London, England)*, *9*(2), R60–R65. https://doi.org/10.1186/cc3023

23. *Meiyazhagan, G., Raju, R., Winfred, S. B., Mannivanan, B., Bhoopalan, H., Shankar, V. ... et al., (2015).* Bioactivity Studies of β-Lactam Derived Polycyclic Fused Pyrroli-Dine/Pyrrolizidine Derivatives in Dentistry: In Vitro, In Vivo and In Silico Studies. *PloS one*, *10*(7), e0131433. https://doi.org/10.1371/journal.pone.0131433 .

24. *Milo, S., Nzakizwanayo, J., Hathaway, H. J., Jones, B. V., & Jenkins, A. T. A. (2019).* Emerg-

ing medical and engineering strategies for the prevention of long-term indwelling catheter blockage. Proceedings of the Institution of Mechanical Engineers. Part H, Journal of engineering in medicine, 233(1), 68–83. https://doi.org/10.1177/0954411918776691

25. *Mitchell, B., Curryer, C., Holliday, E., Rickard, C. M., & Fasugba, O. (2021).* Effectiveness of meatal cleaning in the prevention of catheter-associated urinary tract infections and bacteriuria: an updated systematic review and meta-analysis. *BMJ open*, *11*(6), e046817. https://doi.org/10.1136/bmjopen-2020-046817

26. *Pacios, O., Fernández-García, L., Bleriot, I., Blasco, L., González-Bardanca, M., López, M. ... et al., (2021).* Enhanced Antibacterial Activity of Repurposed Mitomycin C and Imipenem in Combination with the Lytic Phage vB_KpnM-VAC13 against Clinical Isolates of Klebsiella pneumoniae. *Antimicrobial agents and chemotherapy*, *65*(9), e0090021. https://doi.org/10.1128/AAC.00900-21

27. *Pelling, H., Nzakizwanayo, J., Milo, S., Denham, E. L., MacFarlane, W. M., Bock, L. J., Sutton, J. M., & Jones, B. V. (2019)*. Bacterial biofilm formation on indwelling urethral catheters. *Letters in applied microbiology*, *68*(4), 277–293. https://doi.org/10.1111/lam.13144

28. *Pertusati, F., Pileggi, E., Richards, J., Wootton, M., Van Leemputte, T., Persoons, L. ... et al., (2020).* Drug repurposing: phosphate prodrugs of anticancer and antiviral FDA-approved nucleosides as novel antimicrobials. *The Journal of antimicrobial chemotherapy*, *75*(10), 2864–2878. https://doi.org/10.1093/jac/dkaa268

29. *Poyil M.M., Bari M.D.N. (2023).* Repurposing the drug duloxetine for its antibacterial activity against catheter associated urinary tract infections. *The New Armenian Medical Journal*. 17(1): 54-62. https://doi.org/10.56936/18290825-2023.17.54-62

30. *Rahuman, H. B. H., Dhandapani, R., Palanivel, V., Thangavelu, S., Paramasivam, R., & Muthupandian, S. (2021).* Bioengineered phytomolecules-capped silver nanoparticles using Carissa carandas leaf extract to embed on to urinary catheter to combat UTI pathogens. *PloS one*, *16*(9), e0256748. https://doi.org/10.1371/journal.pone.0256748

31. *Shi, D., Hao, H., Wei, Z., Yang, D., Yin, J., Li, H. ... et al., (2022).* Combined exposure to non-antibiotic pharmaceutics and antibiotics in the gut synergistically promote the development of multi-drug-resistance in *Escherichia coli*. *Gut microbes*, *14*(1), 2018901. https://doi.org/10.1080/19490976.2021.2018901

32. *Sievert, D. M., Ricks, P., Edwards, J. R., Schneider, A., Patel, J., Srinivasan, A. ... et al., (2013).* Antimicrobial-resistant pathogens associated with healthcare-associated infections: summary of data reported to the National Healthcare Safety Network at the Centers for Disease Control and Prevention, 2009-2010. *Infection control and hospital epidemiology*, *34*(1), 1–14. https://doi.org/10.1086/668770

33. *Smith, D. R. M., Pouwels, K. B., Hopkins, S., Naylor, N. R., Smieszek, T., & Robotham, J. V. (2019).* Epidemiology and health-economic burden of urinary-catheter-associated infection in English NHS hospitals: a probabilistic modelling study. *The Journal of hospital infection*, *103*(1), 44–54. https://doi.org/10.1016/j.jhin.2019.04.010

34. *Thangamani, S., Younis, W., & Seleem, M. N. (2015).* Repurposing ebselen for treatment of multidrug-resistant staphylococcal infections. Scientific reports, 5, 11596. https://doi.org/10.1038/srep11596

35. *Trautner B. W. (2010).* Management of catheter-associated urinary tract infection. *Current opinion in infectious diseases*, *23*(1), 76–82. https://doi.org/10.1097/QCO.0b013e328334dda8

36. *Vidhya Ganesan, Gowri Meiyazhagan, Muthu Devaraj, Sangeetha Kandasamy, Prasath Manogaran, Govindan Suresh Kumar ... et al., (2022).* ACS Biomaterials Science & Engineering 2022 8 (2), 682-693. https://doi.org/10.1021/acsbiomaterials.1c01481

37. *Zeng, X., She, P., Zhou, L., Li, S., Hussain, Z., Chen, L., & Wu, Y. (2021).* Drug repurposing: Antimicrobial and anti-biofilm effects of penfluridol against Enterococcus faecalis. *MicrobiologyOpen*, *10*(1), e1148. https://doi.org/10.1002/mbo3.1148

38. *Zhu Z, Wang Z, Li S, Yuan X. (2019).* Antimicrobial strategies for urinary catheters. Journal of Biomedical Materials Research Part A. Feb;107(2):445-67. https://doi.org/10.1002/jbm.a.36561

THE NEW ARMENIAN MEDICAL JOURNAL
Volume18 (2024). Issue 1

CONTENTS

THE NEW ARMENIAN MEDICAL JOURNAL

Volume18 (2024). Issue 1

The Journal is founded by
Yerevan State Medical
University after M. Heratsi.

Address for correspondence:

Yerevan State Medical University
2 Koryun Street, Yerevan 0025,
Republic of Armenia

Phones:

(+37410) 582532 YSMU
(+37493 588697 Editor-in-Chief
Fax: (+37410) 582532
E-mail:namj.ysmu@gmail.com, ysmiu@mail.ru
URL:http//www.ysmu.am

Our journal is registered in the databases of Scopus, EBSCO and Thomson Reuters (in the registration process)

SCOPUS EBSCO
REUTERS

Copy editor: Tatevik R. Movsisyan

Printed in "LAS Print" LLC
Director: Suren A. Simonyan
Armenia, 0023,Yerevan,
Acharyan St. 44 Bulding,
Phone: (+374 10) 62 76 12,
E-mail: las.print@yahoo.com