THE NEW ARMENIAN MEDICAL JOURNAL
Volume17 (2023), Issue 1 p. 54-62

DOI: https://doi.org/10.56936/18290825-2023.17.54-62

REPURPOSING THE DRUG DULOXETINE FOR ITS ANTIBACTERIAL ACTIVITY AGAINST CATHETER ASSOCIATED URINARY TRACT INFECTIONS

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Received 15.12.2022; accepted for printing 10.01.2023

Abstract

Catheter associated urinary tract infection is an important nosocomial infection that can be involved by one or more parts of the urinary system including bladder, ureters, urethra and kidneys. The infection is common as studies estimated that the mean incidence of catheter associated urinary tract infection per 1000 catheter-days was as high as 9.86, and when the infection is caused by multidrug resistant bacteria, it can lead to severe sufferings to the patients with longer morbidity and higher medical expenses.

Many of the catheter associated urinary tract infection causing bacteria are known to form biofilms and pathogens like Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, Proteus mirabilis, Enterococcus faecalis etc. are among the most notorious. As such biofilms are extremely resistant to ant external physical, chemical or biological agents, the treatment against them pose serious challenges.

Present study analyses the antibacterial activity of a repurposing anti-depression drug duloxetine against two of the most prevalent catheter associated urinary tract infection causing bacterial pathogens – viz. Escherichia coli and Enterococcus faecalis. Duloxetine showed antibacterial and the lowest inhibitory concentration was found to be 37.5 µg/ml for both microbes. It was also evaluated for their effect against microbial colonization and biofilm formation. The duloxetine didn't allow the microbial colorization up to its minimum inhibitory concentration thus the biofilm reduction was observed as 64% and 86% for Escherichia coli and Enterococcus faecalis respectively. To prevent biofilm formation on urinary catheters, the drug was coated with silicone catheter tube and exhibited antibacterial activity against Escherichia coli and Enterococcus faecalis.

Study suggested that duloxetine can be an effective antibacterial agent against Escherichia coli and Enterococcus faecalis.

Keywords: *duloxetine, catheter, multidrug, biofilm formation, bladder model.*

Introduction

Infections that occur in the urinary tract are common and can range from uncomplicated to severe infections affecting over several million people worldwide [*Flores-Mireles A et al., 2015; Tandogdu Z, Wagenlehner F, 2016; Papanikolopoulou A et al., 2022*]. The earlier report says, the urinary tract infections are third most important cause for nosocomial infection which is regularly related to

Cite This Article as:

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 DOI: https://doi.org/10.56936/18290825-2023.17.54-62

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indwelling catheter usage resulting high morbidity and mortality rate [*Flores-Mireles A et al., 2019; Medina M, Castillo-Pino E, 2019; Skelton-Dudley F et al., 2019*]. Unfortunately, the catheters allowed the urobacteria to adhere on their surface and form the biofilm which may lead to catheter associated urinary tract infection (CAUTI) when the bacteria enter into urinary tract by catheter insertion or through the drainage system [*Feneley R et al., 2012; Newman D et al., 2016; Vergidis P, Patel R, 2012*]. With prolonged insertion of the catheter, the risk of bacteriuria increases, which leads to additional complications, such as septicemia [*Lo E et al., 2014*].

Catheter associated urinary tract infection involves both gram-positive and gram-negative bacterial colonization and their biofilm formation on catheters surface. The *Escherichia coli* and *Enterococcus faecalis* are most prevalent organisms causing CAUTI and makes the management of CAUTI is very difficult owing to its biofilm forming ability and resistance to existing antibiotics [*Bjarnsholt T, 2013; Sharma G et al., 2016*]. Biofilms often decreases the antibiotic susceptibility due to the extracellular polymeric substances protective effect, efflux pumps which force out the antimicrobial compound and the transfer of antibiotic resistance genes in bacterial cells. Therefore, the management of CAUTI is ineffective due to rising of the biofilm thereby prevalence of antibiotic resistance pathogens [*Balcazar J et al., 2015; Karigoudar R et al., 2019; Walker J et al., 2020*]. Consequently, there is an urgent call for the development of new antimicrobial agent with anti-infective property against microbial colonization and biofilm formation of microbes involved in CAUTI. This development process is time consuming and quite expensive, requiring many clinical trials before being released to the market. Hence, in this study, the antibacterial activity of a repurposing drug duloxetine against *Escherichia coli* and *Enterococcus faecalis* and its activity against bacterial colonization and biofilm formation were evaluated.

Repurposing the old drug for new application is one approach gains many attentions as exclusive method for new antimicrobial development. This approach is mainly based on discovering the novel application which is not their original scope of the drug indication [*Thangamani S et al., 2015*]. Because these drugs have been already undergone many clinical trials in humans and their safety, efficacy and pharmacological profiles are known which reduces the time and cost as well as it often reduces the risk involved in antibiotic innovation [*Chong C, Sullivan D, 2007; Thangamani S et al., 2015*]. Considering all these facts, an attempt was made to repurpose the non-microbial drug as antibacterial agent. This study, evaluated the antibacterial activity of duloxetine, an anti-depression drug was evaluated against the most prevalent microbes involved in CAUTI and also evaluated for their ability to prevent colony formation as well as biofilm eradication.

MATERIALS AND METHODS

Mueller Hinton agar from Hi Media was used throughout the study to culture the organism. Rifampicin used as positive control for *Escherichia coli* and ampicillin used as positive control for *Enterococcus faecalis.* Culture without treatment served as negative control.

Determination of antibacterial activity: To establish the antibacterial activity of duloxetine against *Enterococcus faecalis and Escherichia coli,* the well diffusion method was adopted as described earlier [*Gowri M et al., 2016*]. The Mueller Hinton agar and the overnight cultures of *Enterococcus faecalis* and *Escherichia coli* were adjusted to 0.5 MacFarland unit was used for the antibacterial activity. The prepared sterile Mueller-Hinton agar plates were swabbed with the above-mentioned cultures and the wells were drilled. The various concentrations of duloxetine (125 *µg/ml*, 150 *µg/ml*, 200 *µg/ml*) were loaded in each well and incubated for 24 hours. After incubation, the plates were observed for the activity. The antibacterial activity of duloxetine was determined based on the width of the zone of inhibition. The experiments were done in duplicates.

To overcome it is possible, due to the uniting the knowledge and will of all doctors in the world

Minimum inhibitory concentration determination: To ascertain the Minimum Inhibitory Concentration of duloxetine against *Enterococcus faecalis* and *Escherichia coli,* the micro dilution method was implemented as illustrated previously [*Gowri M et al., 2016*]. Here, Mueller-Hinton broth used to culture the microbes. Two-fold serial dilutions of duloxetine (300-2.3 *µg/ml*) were prepared using 200 *µl* of Mueller-Hinton broth in 96 well plates. 20 *µl* of each culture was added to each well and incubated for 24 hours. Plate incubation was monitored turbidity and the optical density was measured at 600 nm using a spectrophotometer. The experiments were carried out in triplicate.

Duloxetine effect on colony formation: To determine the duloxetine effect on *Escherichia coli* and *Enterococcus faecalis* colonization, the culture was used to grow in Mueller-Hinton broth using 96 well plate. Two-fold serial dilutions of duloxetine (300-2.3 *µg/ml*) were prepared using 200 *µl* of Mueller-Hinton broth in 96 well plates. 20 *µl* of each culture was added to each well and incubated for 96 hours. After incubation, each well was washed with phosphate-buffered saline to remove the non-adherent cells and the colonies were fixed with methanol for 30 *mins* followed by staining with 0.1% crystal violet for 45 *mins*. Then, the excess stain was removed by washing followed by air drying. 200 *µl* of mixture of ethanol and acetone was added and the plate was read at 570 *nm* using spectrophotometer. The experiments were done in triplicates.

Duloxetine effect on biofilm formation: To establish the duloxetine effect on *Escherichia coli* and *Enterococcus faecalis* biofilm, the biofilm formation assay was performed in 12 well polystyrene microtiter plates as described earlier [*Gowri M et al., 2020*]; 2 *ml* of bacterial cultures were added into respective wells and incubated for 96 hours to allow the biofilm formation. After incubation, the drug was added at their 1X minimum inhibitory concentration (MIC) (37.5 *µg/ml*) and 2X MIC (75 *µg/ml*) concentrations and incubated for 24 hours. After treatment, each well was washed with phosphate-buffered saline to remove the non-adherent cells and the colonies were fixed with methanol for 30 *mins* followed by staining with 0.1% crystal violet for 45 *mins*. Then, the excess stain was removed by washing followed by air drying. 200 *µl* of mixture of ethanol and acetone was added and the plate was read at 570 *nm* using spectrophotometer. The experiments were done in triplicates.

In vitro bladder model: The *in vitro* bladder model was used to determine the antibacterial activity of duloxetine coated catheters against *Escherichia coli* and *Enterococcus faecalis* as per standard protocols [*Goda R et al., 2022*]. The sterile catheter tube was cut into small pieces and the pieces were dipped into 25 *mg/ml* of duloxetine solution for 30 *mins*. Then, the drug coated tube pieces were air dried. The sterile Mueller-Hinton agar plates were swabbed with respective microbes and the air-dried catheter piece was placed on the surface of plates and incubated for 24 *hours*. After incubation, the plates were observed for zone of inhibition. The experiments were done in duplicates.

Statistical analysis: Mean and standard deviations were calculated for minimum inhibitory concentration determination, colony formation, biofilm formation assays.

RESULTS

Determination of antibacterial activity: The antibacterial activity of a repurposing anti-depression drug duloxetine was determined against *Escherichia coli* and *Enterococcus faecalis* at various concentrations. The antibacterial activity of duloxetine was determined against prevalent microbes involved in CAUTI and measured zone of inhibitions are presented in figure 1 and table. As seen in figure 1, the duloxetine showed activity at 125 *µg*

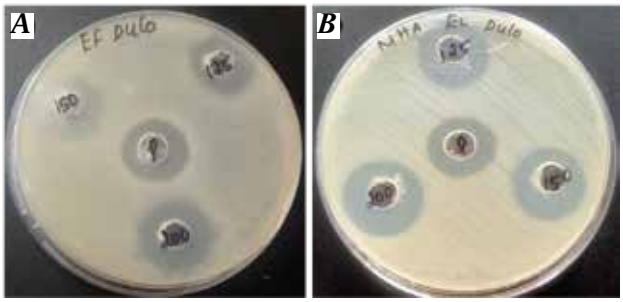

FIGURE 1*. Zones of growth inhibition exhibited by duloxetine: A) Enterococcus faecalis B) Escherichia coli.*

TABLE

Antibacterial activity of duloxetine

Mikroorganisms	Zone of inhibition (*mm*)		
	125 *µg*	150 *µg*	200 *µg*
Enterococcus faecalis	19	20	20
Escherichia coli	18	19	19

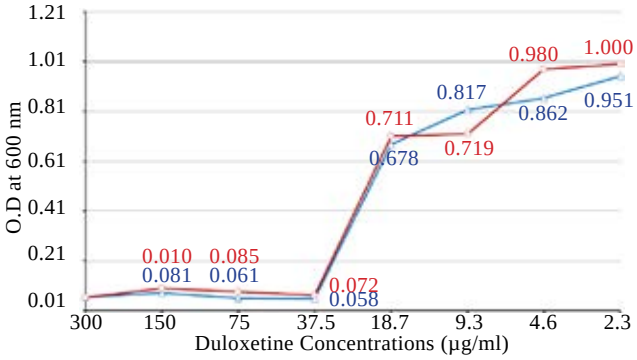

***FIGURE 3**. Pictorial representation minimum inhibitory concentration of duloxetine: A) Enterococcus faecalis round marks), B) Escherichia coli triangular marks)*

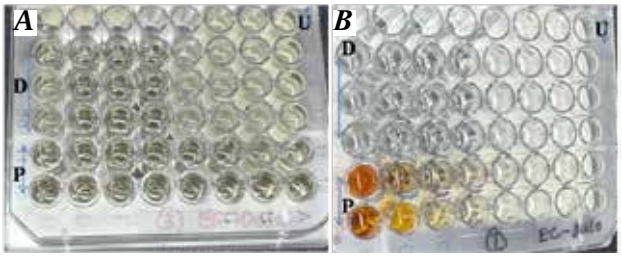

***FIGURE 2**. Minimum inhibitory concentration of duloxetine against Enterococcus faecalis and Escherichia coli*

against both the organism. This shows that, the activity was increased while increasing the concentration against both microbes.

Minimum inhibitory concentration determination: The MIC of duloxetine against *Escherichia coli* and *Enterococcus faecalis* was determined using micro dilution method and the obtained results are presented in Figure 2 and 3. Here, MIC indicates the lowest concentration of particular drug which inhibit the growth of respective bacteria was calculated. As shown in figure 2, the calculated MIC of duloxetine was 37.5 *µg/ml* against both *Escherichia coli* and *Enterococcus faecalis*.

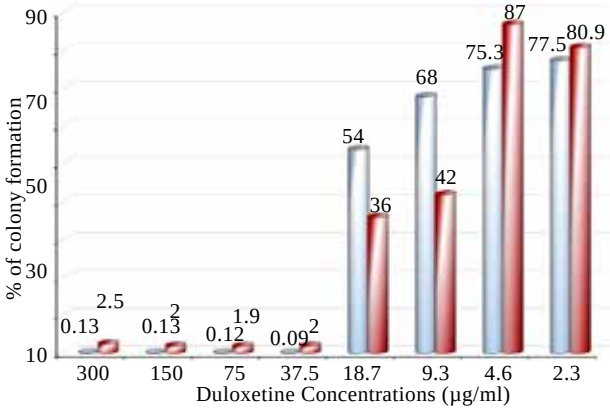

***FIGURE 4** Duloxetine effect on Enterococcus faecalis(left columns) and Escherichia coli (right columns) colony formation*

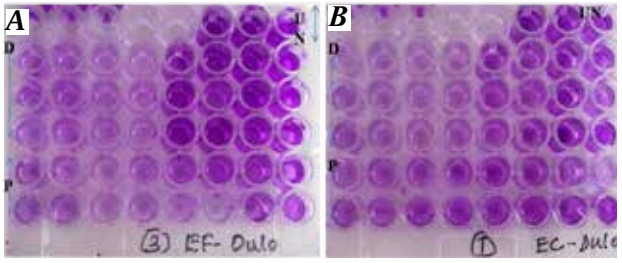

***FIGURE 5**. Pictorial representation of duloxetine effect on colony formation: A) Enterococcus faecalis, B) Escherichia coli*

Duloxetine effect on colonization: The duloxetine effect on *Escherichia coli* and *Enterococcus faecalis* colonization was studied using 96 micro titre plate and the obtained results are interpreted in figures 4 and 5. As mentioned in Figure 5, the duloxetine does not allow the bacteria to grow and form colonies on polystyrene surfaces up to its MIC. With decreasing concentration, colonies were formed on the surfaces, while the formation of colonies was observed, which was reflected in the result. The result indicates the duloxetine potency to destroy the colony forming ability of *Escherichia coli* and *Enterococcus faecalis.*

Anti-biofilm activity of Duloxetine: The duloxetine effect on *Escherichia coli* and *Enterococcus*

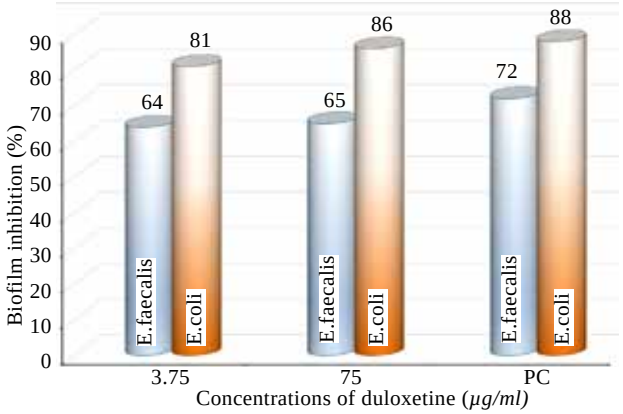

***FIGURE 6**. Effect of Duloxetine on biofilm formation by Enterococcus faecalis and Escherichia coli. Note: PC-Positive control*

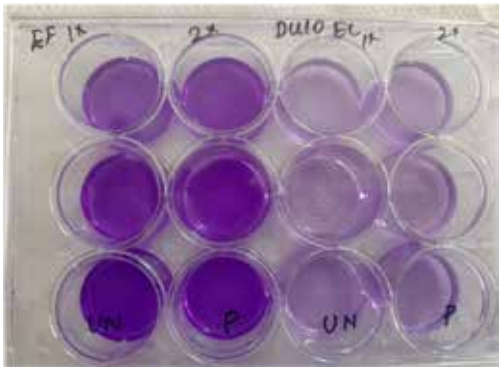

***FIGURE 7**. Pictorial representation duloxetine effect on biofilm formation: A) Enterococcus faecalis, B) Escherichia coli*

faecalis biofilm formation was quantified after treatment with different concentrations and the results are presented in figures 6 and 7. As indicated in figure 4, duloxetine showed 64% and 65% of biofilm reduction against *Enterococcus faecalis* whereas 81% and 86% of biofilm reduction was observed against *Escherichia coli*. It shows the ability of duloxetine in eradicating biofilm formation of *Escherichia coli* and *Enterococcus faecalis.*

Antibacterial activity of duloxetine coating: The antibacterial activity of duloxetine coated catheter tube was evaluated against *Escherichia coli* and *Enterococcus faecalis* using dip and dry method and the obtained result is presented in figure 8. As seen in this figure, the clear zone of inhibition was observed in drug coated catheter tube against both *Escherichia coli* and *Enterococcus faecalis.*

DISCUSSION

Catheter associated urinary tract infections represent an important nosocomial infection which creates considerable clinical challenges. Naturally, these infections are polymicrobial in their structure and are regularly connected to multi drug resistance and biofilm formation which makes treatment challenge [*Ansari M et al., 2020; Sanchez B et al., 2022*]. Hence, in this study the antibacterial activity of a repurposing anti-depression drug duloxetine against the most prevalent organisms *Escherichia coli* and *Enterococcus faecalis* involved in CAUTI was examined. Repurposing an old drug with well-known pharmacology and toxicology profile executed for new application is a new approach to decrease the cost, time as well as risk related to antibiotic innovation. Here, the duloxetine antibacterial activity was evaluated against *Escherichia coli* and *Enterococcus faecalis* and exhibited their activity against both microbes. Consequently, the lowest concentration which inhibits the growth of both *Escherichia coli* and *Enterococcus faecalis* was determined as 37.5 *μg/ml*. Our study was correlated with previous report in which sertraline showed antibacterial effect against *Escherichia coli* in combination with tetracycline [*Kromann S et al., 2019*]. Our study was supported by previous study wherein a repurposing ebselen (organoselenium compound) showed excellent activity against both methicillin and vancomycin resistant *Staphylococcus aureus* by inhibiting the protein synthesis and toxin production [*Thangamani S et al., 2015*]. A study from Muhammad group investigated the anti-depression drug sertraline against various microbes including *Escherichia coli, Pseudomonas aeruginosa, Enterococcus faecalis* and *Acinetobacter baumannii* [*Muhammad A et al., 2015*]. A recent study reported the antibacterial activity of repurposing drugs such as amlodipine, azelastine, ebselen and sertraline against multidrug resistant *S. aureus* and the MIC of amlodipine was 64 *μg/ml*, sertraline showed 20 *μg/ml*, azelastine exhibited 200 μg/ml and ebselen showed 0.25 *μg/ml* [*Natalie K et al., 2021]*. Ahmet group investigated the antibacterial activity of sertraline against various clinically relevant organisms including *Escherichia coli* and *Enterococcus faecalis* [*Ahmet Y et al., 2009*].

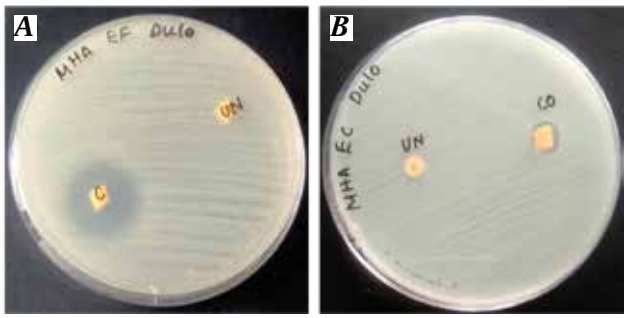

FIGURE 8*. Antibacterial activity of duloxetine coated urinary catheter tube: A) Enterococcus faecalis, B) Escherichia coli*

Besides the antibacterial activity of duloxetine, the drug was evaluated for microbial colonization and biofilm formation. The CAUTI are initiated when the bacteria enter into the catheter during the insertion followed by adhesion of microbes on the surface of catheter resulting microbial colonization leading biofilm formation which is critical for CAUTI treatment [*Arnoldo L et al., 2013; Zhu Z et al., 2019*]. After the adherence of urobacteria on the surfaces, produced dense complex biofilm connected to microbial polysaccharides, host products and extracellular materials. These complex structures protect the bacteria from host defence mechanism, escaped from the regular antibiotic activity [*Pelling H et al., 2019*]. As a consequence, biofilms are not eradicated easily because of the gene transfer between the resistant and non-resistant strains resulting antibiotic resistant biofilm development which act as the reservoir for development of patho-

gens which makes treatment critical. In this regard, our results revealed the ability of duloxetine to eliminate microbial colonization, as well as the formation of E*scherichia coli* and *Enterococcus faecalis* biofilms. In approaching biofilm prevention, it is necessary to focus on each stage of biofilm development from attachment to maturation. [*Koo H et al., 2017; Roy R et al., 2018; Ghosh A et al., 2020; Muhammad M et al., 2020*]. The first stage of biofilm formation is the attachment; hence our study pointed out the duloxetine effect on microbial colonization. Here, the duloxetine does not allow the microbial colonization of both *Escherichia coli* and *Enterococcus faecalis* at its MIC level, when the concentration decreases the microbial colonization was increased. Followed by duloxetine effect on biofilm formation of *Escherichia coli* and *Enterococcus faecalis* was determined and inhibited the *Escherichia coli* and *Enterococcus faecalis* biofilm formation after treatment.

Besides the anti-biofilm activity of duloxetine, the drug was exposed for coating the catheter tube to prevent biofilm development on the inner and outer surface of the catheter surfaces. The coating of anti-biofilm agent on the inner and outer surface is an excellent method to prevent biofilm formation. To test the duloxetine efficacy of coated catheter, we have adopted the *in vitro* bladder model to mimic the common process in a suitable environment. Here, the silicone urinary catheter tube was coated with duloxetine to study the efficacy of the drug. Our findings showed the efficacy of duloxetine in coated catheters as zone of inhibition around the tubes. It indicates that the activity of duloxetine which suppress the growth of *Escherichia coli* and *Enterococcus faecalis* in the surrounding environment whereas the uncoated catheter tube showed no inhibition around the tubes. Our study was correlated with previous results wherein the silicone catheter tube was coated with silver nanocomposite exhibited excellent antibacterial activity against *Escherichia coli* and *S. aureus* and also reduce the bacterial adherence and biofilm formation [*Shuai Z et al., 2019; Rahuman H et al., 2021*]. Similarly, antibacterial activity of oral fosfomycin was evaluated against *Enterococcus faecalis* using *in vitro* bladder infectious model wherein the fosfomycin showed excellent activity at its MIC level and found that the fosfomycin was able to suppress the re-growth of the *Enterococcus faecalis* [*Abbott I et al., 2020*]. Likewise, a study reported the ability of new agents benzalkonium chloride, gluteraldehyde and polyacrylic acid that prevents the biofilm formation on coating silicone catheter against *Escherichia coli* and *Pseudomonas. aeruginosa*. Initially, they have studied the ability on biofilm formation in three various urine catheters made of silicone, red rubber and polyvinyl chloride. The result revealed that the antibiofilm agent was effectively inhibiting the biofilm formation formed on silicone catheter tube [*Navarro S et al., 2022*]. Likewise, Henly E. and co-authors (2019) studied the biocides coating catheter against most prevalent microbes involved in CAUTI.

Conclusion

The present study highlights the antibacterial activity of the reused antidepressant duloxetine against *Escherichia coli* and *Enterococcus faecalis*, which are predominantly involved in CAUTI. Therefore, duloxetine exhibited antibacterial against both microbes and also inhibited colony formation thereby reduction of biofilm formation was observed. It also showed the antibacterial activity when the catheter was coated with duloxetine against both microbes. All the results suggested that duloxetine can be better antibacterial agent for CAUTI.

Acknowledgement: *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 IJ, van Gorp E, van der Meijden A, Wijma RA, Meletiadis J, Roberts JA. et al. (2020).* Oral fosfomycin treatment for enterococcal urinary tract infections in a dynamic *in vitro* model. Antimicrob Agents Chemother. 2020, 64: 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, 43(4): 651-656. https://pubmed.ncbi.nlm.nih.gov/20084919/

3. *Ansari MA, Albetran HM, Alheshibri MH, Timoumi A, Algarou NA, Akhtar S, Slimani Y. et al. (2020).* Synthesis of Electrospun TiO_2 Nanofibers and Characterization of Their Antibacterial and Antibiofilm Potential against Gram-Positive and Gram-Negative Bacteria. Antibiotics (Basel). 2020 Sep 3. 9:572. doi: https://doi.org/10.3390/antibiotics9090572
4. *Arnoldo L, Migliavacca R, Regattin L, Raglio A, Pagani L, Nucleo E. et al. (2013).* Prevalence of urinary colonization by extended spectrum-beta-lactamase Enterobacteriaceae among catheterised inpatients in Italian long term care facilities. BMC Infect Dis. 2013, 13:124. https://doi.org/10.1186/1471-2334-13-124
5. *Balcazar JL, Subirats J, Borrego CM. (2015).* The role of biofilms as environmental reservoirs of antibiotic resistance. Front Microbiol. 2015, 6:1216. https://doi.org/10.3389/fmicb.2015.01216.
6. *Bjarnsholt T. (2013).* The role of bacterial biofilms in chronic infections. APMIS Suppl. 2013, 121:1–51. https://doi.org/10.1111/apm.12099.
7. *Chong CR, Sullivan DJ Jr. (2007).* New uses for old drugs. Nature. 2007 Aug 9;448. 7154:645-6. doi: https://doi.org/10.1038/448645a
8. *Feneley RC, Kunin CM, Stickler DJ. (2012).* An indwelling urinary catheter for the 21st century. BJU Int. 2012 Jun;109. 12:1746-9. doi: https://doi.org/10.1111/j.1464-410X.2011.10753.x.
9. *Flores-Mireles A, Hreha TN, Hunstad DA. (2019).* Pathophysiology, treatment, and prevention of catheter-associated urinary tract infection. Top Spinal Cord Inj Rehabil. 2019, 25, 228–240. doi: https://doi.org/10.1310/sci2503-228
10. Flores-Mireles AL, Walker JN, Caparon M, Hultgren SJ. (2015). Urinary tract infections: epidemiology, mechanisms of infection and treatment options. Nat Rev Microbiol. 2015, 13:269–284. https://doi.org/10.1038/nrmicro3432.
11. *Ghosh A, Jayaraman N, Chatterji D. (2020).* Small-molecule inhibition of bacterial biofilm. ACS Omega. 2020, 5:3108–3115. https://doi.org/10.1021/acsomega.9b03695
12. *Goda RM, El-Baz AM, Khalaf EM, Alharbi NK, Elkhooly TA, Shohayeb MM. (2022).* Combating Bacterial Biofilm Formation in Urinary Catheter by Green Silver Nanoparticle. Antibiotics. 2022, 11:495. https://doi.org/10.3390/antibiotics11040495
13. *Gowri M, Jayashree B, Jeyakanthan J, Girija EK. (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. J Appl Microbiol. 2020 Feb;128.2:426-437. doi: https://doi.org/10.1111/jam.14490m
14. *Gowri M, Sofi Beaula W, Biswal J, Dhamodharan P, Saiharish R, Rohan PS, Pitani R. 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. Biochim Biophys Acta. 2016 Apr;1860. 4:636-47. doi: https://doi.org/10.1016/j.bbagen.2015.12.020
15. *Henly EL, Dowling JAR, Maingay JB, Lacey MM, Smith TJ, Forbes S. (2019).* Biocide exposure induces changes in susceptibility, pathogenicity, and biofilm formation in uropathogenic *Escherichia coli*. Antimicrob Agents Chemother. 2019, 63: e01892-18. https://doi.org/10.1128/AAC.01892-18
16. *Karigoudar RM, Karigoudar MH, Wavare SM, Mangalgi SS. (2019).* Detection of biofilm among uropathogenic Escherichia coli and its correlation with antibiotic resistance pattern. J Lab Physicians. 2019, 11, 17–22. doi: https://doi.org/10.4103/JLP.JLP_98_18
17. *Koo H, Allan RN, Howlin RP, Stoodley P, Hall-Stoodley L. (2017).* Targeting microbial biofilms: Current and prospective therapeutic strategies. Nat. Rev. Microbiol. 2017, 15, 740–755. https://doi.org/10.1038/nrmicro.2017.99

18. *Kromann S, Hvidtfeldt A, Boye M, Sørensen DB, Jørgensen S, Nielsen JP, et al. (2019).* *In vitro* synergy of sertraline and tetracycline cannot be reproduced in pigs orally challenged with a tetracycline resistant *Escherichia coli*. BMC Microbiol. 2019 Jan 11;19. 1:12. doi: https://doi.org/10.1186/s12866-018-1383-5

19. *Lo E, Nicolle LE, Coffin SE, Gould C, Maragakis LL, Meddings J. et al. (2014).* Strategies to prevent catheter-associated urinary tract infections in acute care hospitals: 2014 update. Infect Control Hosp Epidemiol. 2014 May;35. 5:464-79. doi: https://doi.org/10.1086/675718

20. *Medina M, Castillo-Pino E. (2019).* An introduction to the epidemiology and burden of urinary tract infections. Ther Adv Urol. 2019, 11:1756287219832172. doi: https://doi.org/10.1177/1756287219832172

21. *Muhammad A, Fazal S, Jawad A, Arif-Ullah K, Farhat U, Ihsan U. et al. (2015).* Sertraline enhances the activity of antimicrobial agents against pathogens of clinical relevance. J Biol Res (Thessalon), 2015, Apr 16;22. 1:4. doi: https://doi.org/10.1186/s40709-015-0028-1

22. *Muhammad MH, Idris AL, Fan X, Guo Y, Yu Y, Jin X. et al. (2020).* Beyond risk: Bacterial biofilms and their regulating approaches. Front Microbiol. 2020, 11, 928. https://doi.org/10.3389/fmicb.2020.0092

23. *Natalie KB, Grace CL, Chengwen T, Christopher RF. (2021).* *In vitro* activity of non-antibiotic drugs against Staphylococcus aureus clinical strains. J Glob Antimicrob Resist. 2021 Dec; 27:167-171. doi: https://doi.org/10.1016/j.jgar.2021.09.003

24. *Navarro S, Sherman E, Colmer-Hamood JA, Nelius T, Myntti M, Hamood AN. (2022).* Urinary Catheters Coated with a Novel Biofilm Preventative Agent Inhibit Biofilm Development by Diverse Bacterial Uropathogens. Antibiotics. 2022, 11, 1514. https://doi.org/10.3390/antibiotics11111514

25. *Newman DK, Wyman JF, Welch VW. (2016).* Core Curriculum for Urologic Nursing; Jannetti Publications: Pitman, NJ, USA, 2016.

26. *Papanikolopoulou A, Maltezou HC, Stoupis A, Kalimeri D, Pavli A, Boufidou F. et al. (2022).* Catheter-Associated Urinary Tract Infections, Bacteremia, and Infection Control Interventions in a Hospital: A Six-Year Time-Series Study. J. Clin. Med. 2022, 11, 5418. https://doi.org/10.3390/jcm11185418

27. *Pelling H, Nzakizwanayo J, Milo S, Denham EL, MacFarlane WM, Bock LJ. et al. (2019).* Bacterial biofilm formation on indwelling urethral catheters. Lett Appl Microbiol. 2019 Apr; *68*:4, 277–293. doi: https://doi.org/10.1111/lam.13144

28. *Pelling, H, Nzakizwanayo, J, Milo, S, Denham, EL, MacFarlane, WM, Bock. et al. (2019).* Bacterial biofilm formation on indwelling urethral catheters', Letters in Applied Microbiology, 2019, 68:4, 277-293. https://doi.org/10.1111/lam.13144

29. *Rahuman HBH, 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. 2021 Sep 2. 16:9. e0256748. doi: https://doi.org/10.1371/journal.pone.0256748.

30. *Roy R, Tiwari M, Donelli G, Tiwari V. (2018).* Strategies for combating bacterial biofilms: A focus on anti-biofilm agents and their mechanisms of action. Virulence. 2018 Jan 1. 9:1. 522-554. doi: https://doi.org/10.1080/21505594.2017.1313372

31. *Sanchez BC, Heckmann ER, Green SI, Clark JR, Kaplan HB, Ramig RF. et al. (2022).* Development of Phage Cocktails to Treat *Escherichia coli* Catheter-Associated Urinary Tract Infection and Associated Biofilms. Front. Microbiol. 2022, 13:796132. doi: https://doi.org/10.3389/fmicb.2022.796132

32. *Sharma G, Sharma S, Sharma P, Chandola D, Dang S, Gupta S. et al. (2016).* *Escherichia coli* biofilm: development and therapeutic strategies. J Appl Microbiol. 2016, 121:309 –319. https://doi.org/10.1111/jam.13078.

33. *Shuai Z, Liyun W, Xinjin L, Jan V, Robert K, George C. et al. (2019).* Enhanced Antibacterial and Antiadhesive Activities of Silver-PTFE Nanocomposite Coating for Urinary Catheters. ACS Biomater Sci Eng 2019, 5, 2804−2814. https://doi.org/10.1021/acsbiomaterials.9b00071

34. *Skelton-Dudley F, Doan J, Suda K, Holmes SA, Evans C, Trautner B. (2019).* Spinal cord injury creates unique challenges in diagnosis and management of catheter-associated urinary tract infection. Top Spinal Cord Inj Rehabil. 2019, 25, 331–339. doi: https://doi.org/10.1310/sci2504-331

35. *Tandogdu Z, Wagenlehner FM. (2016).* Global epidemiology of urinary tract infections. Curr Opin Infect Dis. 2016, 29:73–79. https://doi.org/10.1097/QCO.0000000000000228

36. *Thangamani S, Younis W, Seleem MN. (2015).* Repurposing ebselen for treatment of multidrug-resistant Staphylococcal infections. Scienific Reports. 2015. 5. 11596:13. doi: https://doi.org/10.1038/srep11596

37. *Vergidis P, Patel R. (2012).* Novel approaches to the diagnosis, prevention, and treatment of medical device-associated infections. Infect Dis Clin North Am. 2012 Mar. 26. 1:173-86. doi: https://doi.org/10.1016/j.idc.2011.09.012

38. *Walker JN, Flores-Mireles AL, Lynch AJL, Pinkner C, Caparon MG, Hultgren SJ. (2020).* High-resolution imaging reveals microbial biofilms on patient urinary catheters despite antibiotic administration. World J Urol 2020, 38, 2237–2245. doi: https://doi.org/10.1007/s00345-019-03027-8

39. *Zhu Z, Wang Z, Li S, Yuan X. (2019).* Antimicrobial strategies for urinary catheters. J Biomed Mater Res A. 2019 Feb;107(2):445-467. doi: https://doi.org/10.1002/jbm.a.36561

THE NEW ARMENIAN MEDICAL JOURNAL
Volume17 (2023). Issue 1

CONTENTS

THE NEW ARMENIAN MEDICAL JOURNAL

Volume17 (2023). Issue 1

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

SCOPUS EBSCO REUTERS

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Director: Suren A. Simonyan
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