Effect of trichomonacidal peptides LL-37 and KR-12 on vaginal microbiota

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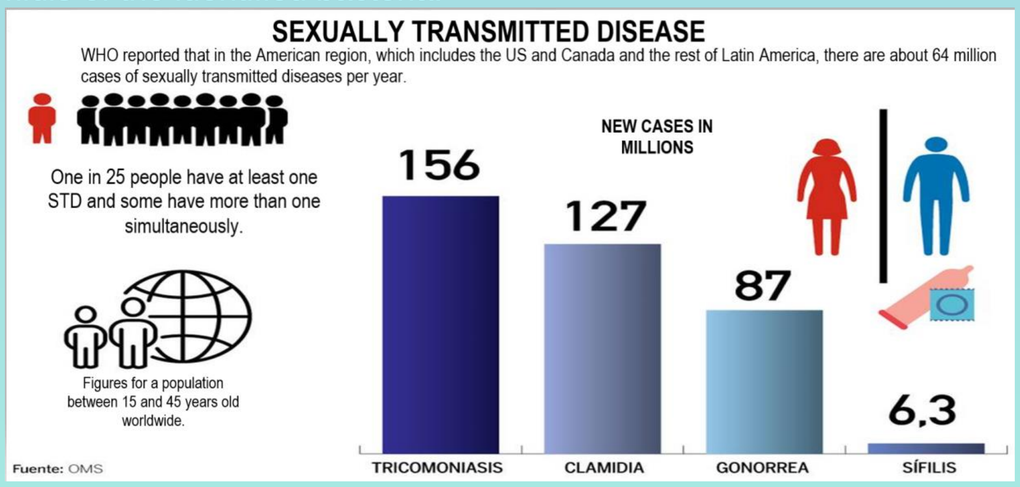
INTRODUCTION

Trichomoniasis is one of the most common non-viral sexually transmitted infections in the world and is caused by the pathogen *Trichomonas vaginalis*. Medications of choice to treat trichomoniasis are the family of nitroimidazoles such as metronidazole. However, the selection of strains of *T. vaginalis* resistant to these drugs has recently been observed. In addition, nitroimidazoles have adverse side effects such as headache, vomiting, and nausea. This makes trichomoniasis a public health problem, and the identification of molecules with potential use for treatment becomes urgent. In this sense, antimicrobial peptides can be attractive, either as an alternative or complementary treatment. Our working group has reported that the antimicrobial peptides LL-37 and KR-12 have trichomonicide activity. The combination of the minimum inhibitory concentration 50 (MIC50) metronidazole with the MIC50 of the antimicrobial peptides practically reduces the parasitic load. However, the consequence on the vaginal microbiota, which is an essential part of maintaining the homeostasis of the genitourinary tract, is unknown, being *Lactobacillus acidophilus* and *Staphylococcus epidermidis* of the identified bacteria.

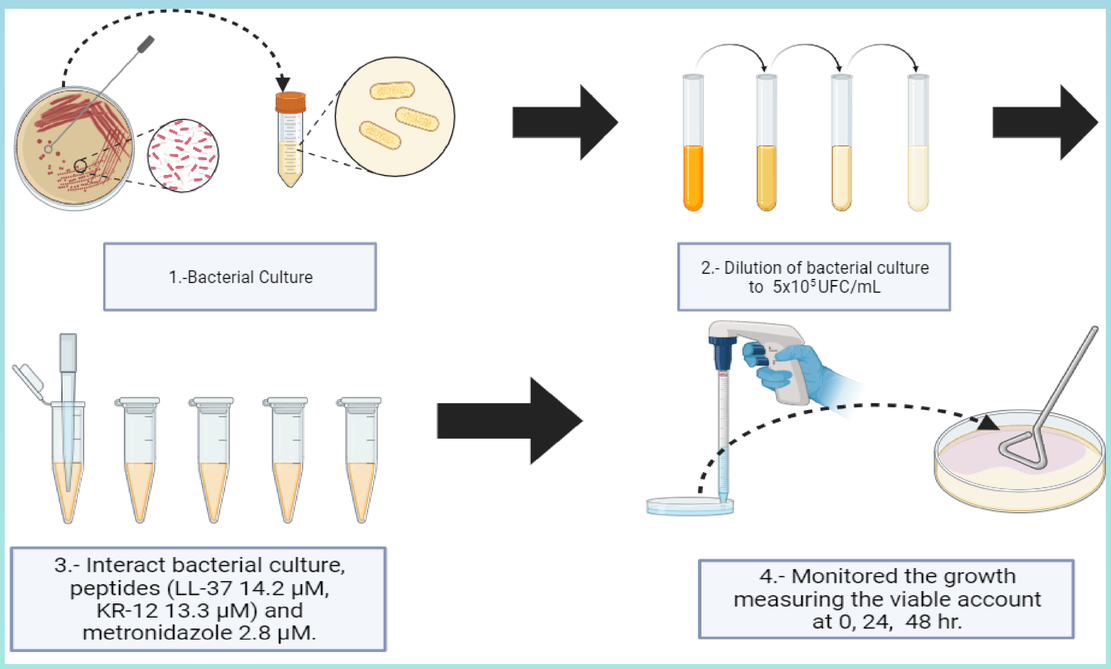


OBJECTIVE

The aim of this study was to analyze the effect of LL-37 and KR-12 peptides in combination with metronidazole on *Lactobacillus acidophilus* and *Staphylococcus epidermidis*.

METHODOLOGY

The viability of the bacteria *L. acidophilus* and *S. epidermidis* was analyzed at 0, 24, y 48 h used MIC 50 of each peptides and in addition metronidazole (MIC50 used against *T. vaginalis* resistant strain).



RESULTS

1. The viability of *L. acidophilus was* stable in interaction with the trichomonicide peptides LL-37 and KR-12 in combination with metronidazole

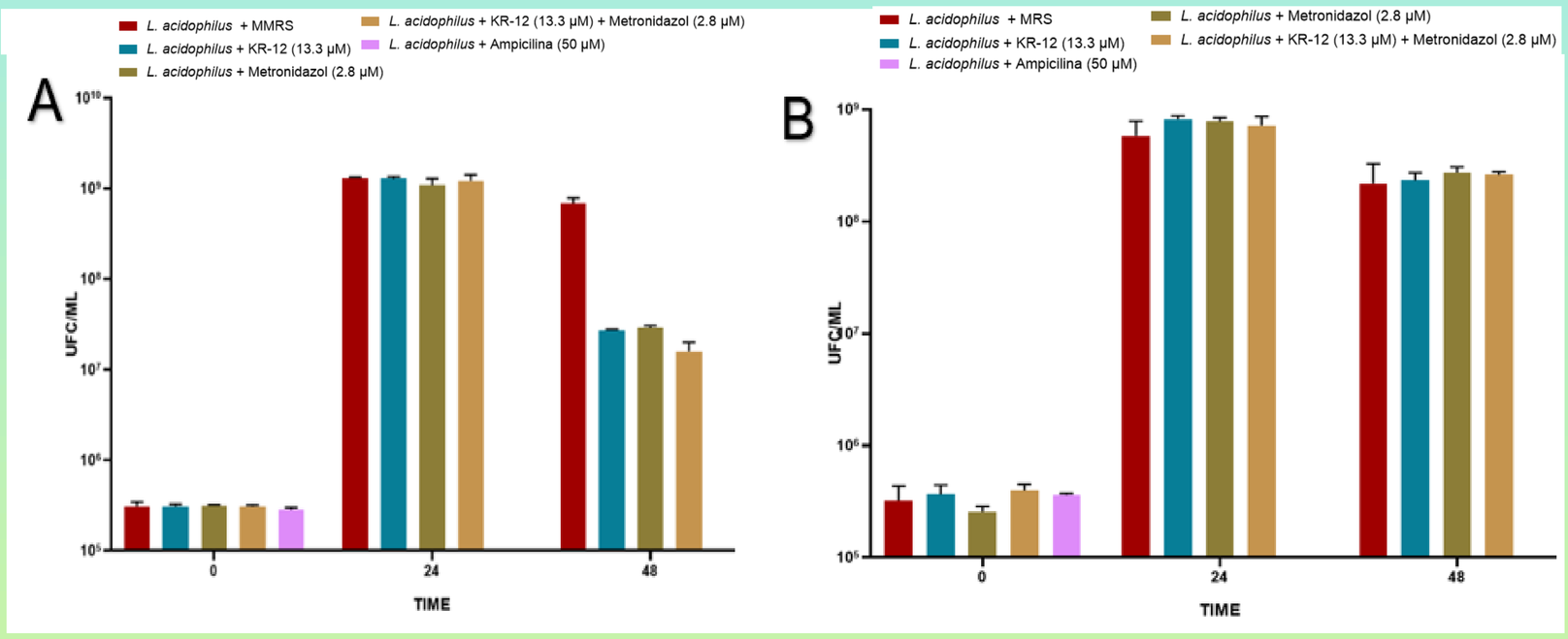


Figure 1. Evaluation of CFUs after treatment of tricomonicide peptides and metronidazole on *L. acidophilus*. A) LL-37 (14.2 µM) and B) KR-12 (13.3 µM). Each peptide was analyzed alone and in combination of metronidazole (2.8 µM) or ampicillin (50 µg/mL) as a control. After 24 y 48 h of growth colonias was counted. The test was performed in triplicate.

2. The effect of the viability of *S. epidermidis* depends on the tricomonicide peptide.

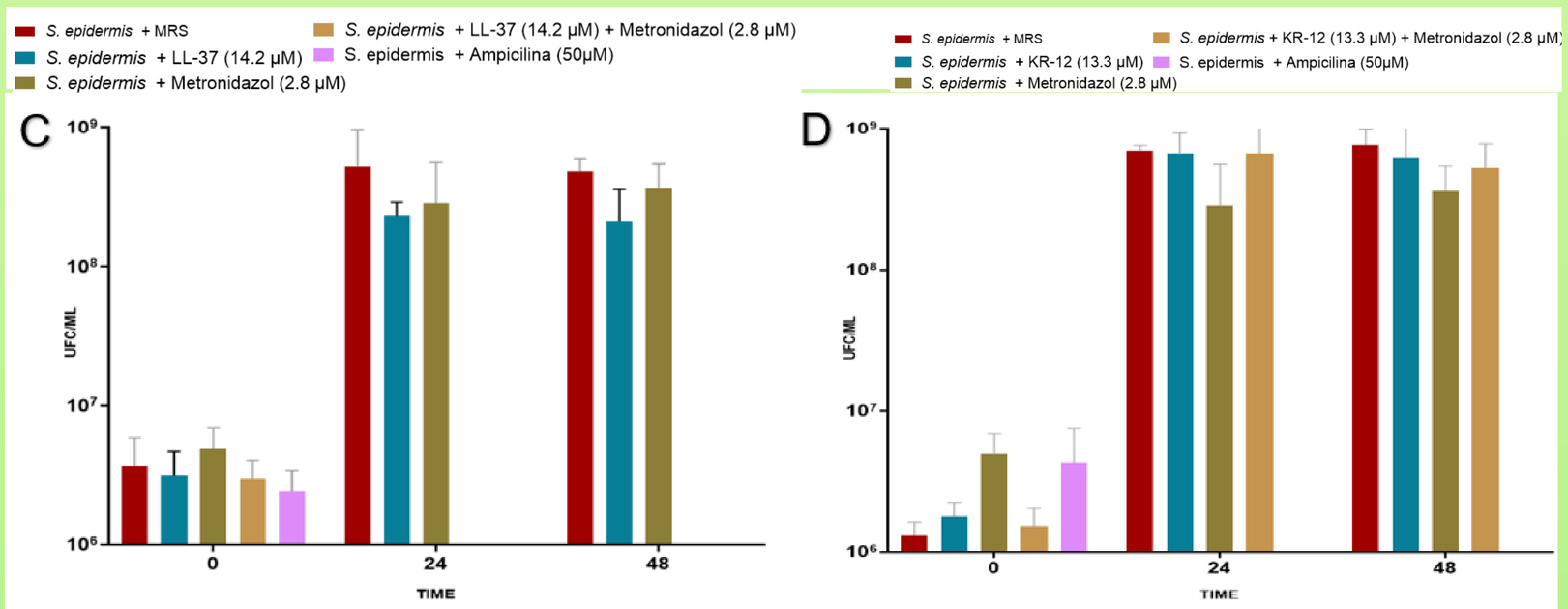


Figure 2. Evaluation of CFUs after treatment of tricomonicide peptides and metronidazole on S. epidermis A) LL-37 (14.2 µM) and B) KR-12 (13.3 µM). Each peptide was analyzed alone and in combination of metronidazole (2.8 µM) or ampicillin (50 µg/mL) as a control. After 24 y 48 h of growth colonias was counted. The test was performed in triplicate

CONCLUSION

- The effect of peptide LL-37 on the viability of *L. acidophilus* decreases by only 20%
- LL-37 in combination with metronidazole has strong inhibition activity (100%) on *S. epidermidis.*
- KR-12 does not affect the viability of either *L. acidophilus* or *S. epidermidis* alone or in combination with metronidazole.
- These results revealed variations between the two peptides, for this we suggest that the peptide KR-12 presents a potential use for treatment in combination with metronidazole against trichomoniasis without affecting the vaginal microbiota

REFERENCES

1. Fichorova RN, et al., The Villain Team-Up or how Trichomonas vaginalis and bacterial vaginosis alter innate immunity in concert Sexually Transmitted Infections 2013;89:460-466.
2. Ramírez-Ledesma, MG, et al., (2022). The antimicrobial peptides LL-37, KR-20, FK-13 and KR-12 inhibit the growth of a sensitive and a metronidazole-resistant strain of Trichomonas vaginalis. Parasitology Research. 121. 10.1007/s00436-022-07674-6.
3. Bechinger, B., & Gorr, S. U. (2017). Antimicrobial peptides: mechanisms of action and resistance. Journal of dental research, 96(3), 254-260.
4. Bendesky, A., & Menéndez, D. (2001). Metronidazol: una visión integral. Rev Fac Med UNAM, 44(6), 255-9.
5. Brotman, R. M., Bradford, L. L., Conrad, M., Gajer, P., Ault, K., Peralta, L., & Ravel, J. (2012). Association between Trichomonas vaginalis and vaginal bacterial community composition among reproductive-age women. Sexually transmitted diseases, 807-812.