Investigating the Effect of Multiple-Antidepressant Exposure on the Evolution of Antibiotic Resistance in *E. coli*

Cole Bell, Paige Borgmeyer, Amanda Korte, Zoya Muellerleile, & Paola Rueda-Irenze

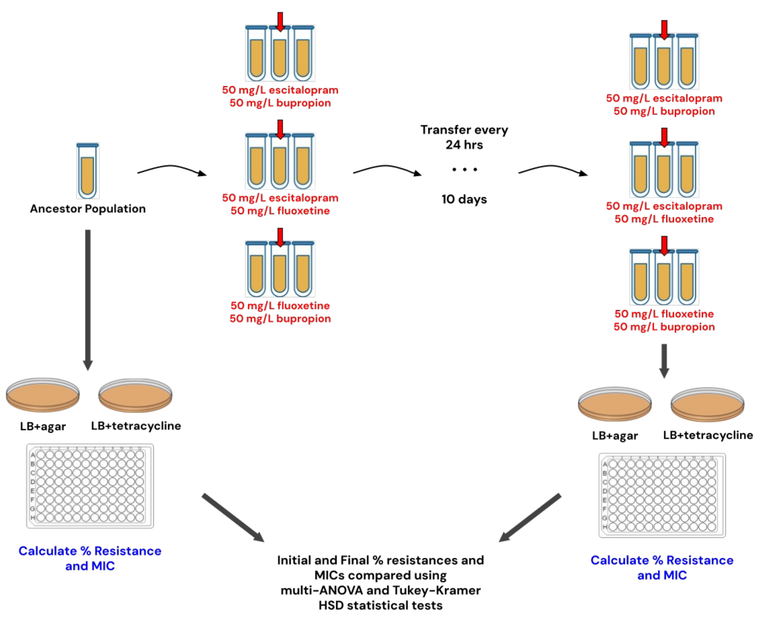
Introduction

<u>Research Question:</u> How does exposure combinations of escitalopram, fluoxetine, and bupropion affect the evolution of antibiotic resistance to tetracycline in *Escherichia coli*?

- Exposure to non-antibiotic pharmaceutical compounds may promote antibiotic resistance in bacteria (Wang et. al, 2020).
- Antidepressants are some of the most prevalent pharmaceutical compounds that contaminate the environment (Castillo-Zacarías et. al, 2021).
- Previous studies have mostly tested the effects of exposure to individual antidepressants on antibiotic resistance, but these compounds coexist simultaneously in the environment and may interact to influence antibiotic resistance.

We hypothesize that the bupropion treatment groups will have the highest percent resistances to tetracycline because their combinations will contain two different classes of antidepressants (SSRIs and SNRIs).

Methods



Results

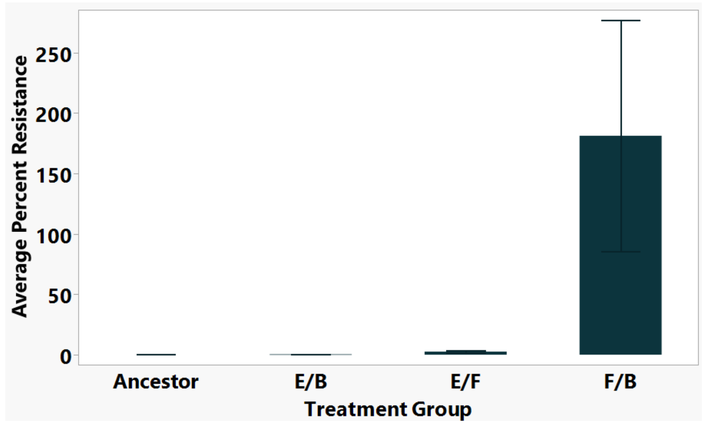


Figure 1. Average percent resistance to tetracycline of *E. coli* populations treated with various combinations of antidepressants. An ancestor population of *E. coli* was used to create three treatment groups, each exposed to either escitalopram/bupropion, escitalopram/fluoxetine, or fluoxetine/bupropion for 10 consecutive days. After 10 days of consecutive exposure, percent resistance to tetracycline was then calculated by obtaining viable counts for each population on traditional LB plates and on LB plates containing 7µg/mL tetracycline. Statistical analysis was performed using a multi-ANOVA test with a p-value threshold of 0.05. Each error represents one standard deviation from the mean. B: bupropion. E: escitalopram. F: fluoxetine.

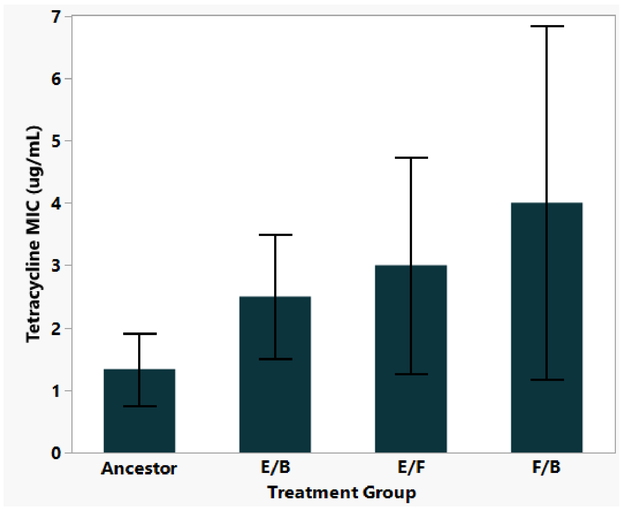


Figure 2. Average minimum inhibitory concentration for tetracycline of *E. coli* populations treated with various combinations of antidepressants. An ancestor population of *E. coli* was used to create three treatment groups, each exposed to either escitalopram/bupropion, escitalopram/fluoxetine, or fluoxetine/bupropion for 10 consecutive days. After 10 days of consecutive exposure, minimum inhibitory concentration assays using tetracycline were performed on each treatment group. Statistical analysis was performed using a multi-ANOVA test with a p-value threshold of 0.05. Each error represents one standard deviation from the mean. B: bupropion. E: escitalopram. F: fluoxetine.

Conclusions

- There was no statistically significant increase in tetracycline MIC for any treatment group.
- There was a statistically significant increase in percent resistance to tetracycline in the *E. coli* population exposed to fluoxetine/bupropion compared to the ancestor population.
  - This is consistent with previous studies showing that exposure to these antidepressants individually promotes antibiotic resistance in *E. coli* (Ding et. al, 2022; Wang et. al, 2023).
- *E. coli* exposed to fluoxetine and bupropion showed a much larger increase in percent resistance compared to the other treatment groups.
  - Fluoxetine/bupropion treated populations showed more growth on tetracycline plates than traditional LB plates, which may be a result of plating error.
  - This result may be influenced by the fact that fluoxetine and bupropion belong to different classes of antidepressants (SSRIs and SNRIs, respectively).
  - This suggests that fluoxetine and bupropion may interact to promote antibiotic resistance in *E. coli*, especially more so than the other combinations tested in this experiment.

Future Directions

- Further explore how the mechanisms of action of these antidepressants may interact to promote antibiotic resistance in *E. coli.*
- Compare tetracycline resistance between *E. coli* populations exposed to antidepressants individually versus in combination.
- Investigate whether exposure to combinations of antidepressants promotes multi-antibiotic resistance more than exposure to individual antidepressants.

Acknowledgements & References

We would like to thank Dr. Catherine Kirkpatrick, Adam Engelhardt, the BIOL3004 Biological Sciences Lab, Amara Carey, Haley Leblanc, and BIOL3004 Lab TAs for giving us the opportunity to conduct this research.