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The in vitro study of the susceptibility of Bifidobacteria to antidepressants

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Abstract

This study aimed to compare the antimicrobial activity of different classes of antidepressants, specifically Brintellix (vortioxetine), a serotonin modulator and stimulator (SMS), and Cipralex (escitalopram) and Seropram (citalopram), both selective serotonin reuptake inhibitors (SSRIs). The effects of these antidepressants on growth kinetics were tested in 22 strains of the genus *Bifidobacterium*. Species were cultivated in TPY liquid medium under anaerobic conditions. Each antidepressant, in its original commercially available liquid form, was added to the culture medium at final concentrations of 200, 400, and 600 µg/mL. Bacterial growth was monitored via OD_{600}, and statistical significance was assessed using the non-parametric Kruskal–Wallis test. Dose-response curves and IC_{50} values were generated to quantify the antibacterial effect. Brintellix demonstrated the strongest antibacterial activity, significantly reducing growth in all 22 strains and showing the lowest mean IC_{50} value. Cipralex induced moderate inhibition, while Seropram had the weakest effect. The results show that antidepressants can differentially affect bifidobacterial growth and suggest that SMS-class drugs may exert stronger antimicrobial actions than traditional SSRIs. Further studies are needed to explore the broader implications of antidepressant use on microbiota composition and host health, and to compare different antidepressant classes.

Introduction

Major depressive disorder (MDD) is a serious mental illness that affects more than 300 million individuals worldwide and is one of the major reasons for disability and low quality of life (Wang et al. 2017; Poggini et al. 2023; Arias-de la Torre et al. 2023). It is characterized by feeling of sadness, anhedonia or loss of interest in previously enjoyable activities, poor concentration, low energy, changes in appetite and sleep, and sometimes even suicidal thoughts (Curley et al. 2023). The prevalence of depression has been increasing, with a notable spike during the COVID-19 pandemic (Jiang et al. 2025). Since then, studies indicate a rise in the number of people experiencing depression and the overall burden of the illness (Winkler et al. 2020; Krulichová et al. 2025). Treatment is based on antidepressant (AD) medication, often in combination with psychotherapy, and its effectiveness depends on the individual response, and the type and severity of depression (Mavranezouli et al. 2024).

Antidepressants are the most commonly used drugs for the treatment of depression (Cipriani et al. 2018). They are categorized into several groups based on their mechanisms of action, including selective serotonin reuptake inhibitors (SSRIs), tricyclic antidepressants, serotonin modulators and stimulators (SMSs), monoamine oxidase inhibitors, and atypical antidepressants (Sheffler et al. 2023). SSRIs are known to inhibit serotonin reuptake in neurones and increase serotonin availability, thereby promoting signalling between neurones (Sarkar et al. 2025). SMSs not only block serotonin reuptake, but also act on multiple serotonin receptors to enhance serotonergic activity (Sheffler et al. 2023). To increase the likelihood of successful treatment, the most suitable class of antidepressants should be selected based on the patient's symptoms, with an appropriate dosage and duration of therapy (Marasine et al. 2021).

Based on the recognised concept of the microbiota-gut-brain (MGB) axis (Morais et al. 2020), the treatment of depression can be supported by probiotic bacteria. The relationship between major depressive disorder and the gut microbiota has recently received considerable attention (Xu et al. 2023). Intestinal bacteria contribute to vital processes such as digestion, immune modulation, and homeostasis (Hou et al. 2022). Notably, they produce beneficial metabolites, especially butyrate (Singh et al. 2023), and neuroactive agents, particularly neurotransmitters and neurotransmitter precursors (Miri et al. 2023).

Among the microorganisms most frequently investigated as probiotics in the context of the gut–brain axis are bifidobacteria and lactic acid bacteria, including species of the genus *Lactobacillus* and related taxa, which have been widely studied for their potential psychobiotic effects (Rocchetti et al. 2025; Chakma et al. 2025). The reviews by Nikolova et al. (2021) and Li et al. (2023) summarise findings on the effects of probiotics on depressed patients focusing mainly on lactobacilli and bifidobacteria. Probiotics appear to be effective in reducing depressive symptoms when combined with antidepressants, however, the application of bacteria as a standalone treatment has not confirmed the desired effect. The differences and inconsistencies in clinical research outcomes are influenced by stage and severity of depression in study participants, as well as by variations in research procedures and approaches.

Another perspective on this issue is provided by *in vitro* studies examining the direct effect of ADs on bacterial cultures. Only a few reports have investigated the growth-inhibitory effects of SSRIs (fluvoxamine, fluoxetine, escitalopram), SNRIs (duloxetine, venlafaxine), and the atypical antidepressant mirtazapine on commensal bacteria such as *S. aureus*, *E. coli*, *C. albicans*, *B. bifidum*, *E. faecalis*, and *L. rhamnosus* (Rukavishnikov et al. 2023). Several *in vitro* analyses have also reported the antimicrobial effects of antidepressants against several individual bacterial strains. For example, selective serotonin reuptake inhibitors (SSRIs) have demonstrated synergistic effects when combined with certain antibiotics against multiple bacterial species (Munoz-Bellido et al. 2000). Sertraline, in particular, has shown strong antibacterial activity and has been reported to enhance the effectiveness of antibiotics (Ayaz et al. 2015). However, most of these studies focus on pathogenic bacteria and do not explore the effects on beneficial gut commensals (Munoz-Bellido et al. 2000; Ayaz et al. 2015; Karine de Sousa et al. 2018). These data are still scarce, and there is a lack of studies evaluating the effects of serotonin modulators and stimulators (SMSs) on individual commensal bacterial strains with beneficial effects, despite their increasing clinical use as probiotics.

The present study therefore aimed to investigate the effects of three antidepressants, Brintellix (vortioxetine), Cipralex (escitalopram) and Seropram (citalopram), on 22 commensal bacterial strains of the genus *Bifidobacterium* isolated from the intestinal tract of adult humans, both healthy (6 strains) and ill (6 strains from patients with inflammatory bowel disease), from children (3 strains), from dental plaque (1 strain), from raw cow's milk (1 strain), and from commercially available probiotic preparations (5 strains).

Material and methods

Bacterial Strains and Culture Conditions

A total of 22 facultative anaerobic bacterial strains, representing seven species of the genus *Bifidobacterium*, were selected for this study (Table S1). Type strains were obtained from recognized international culture collections (DSMZ, ATCC, LMG). Cell morphology, including irregular pleomorphic rods, and culture purity were verified by light microscopy.

Wild bifidobacterial strains were isolated from human intestinal samples as follows. Fresh faecal samples (0.3–1.0 g) were aseptically transferred into Hungate tubes containing anaerobic TPY broth composed of (g/L): peptone (10), glucose (10), yeast extract (5), soya peptone (5), KH_2PO_4 (2), $MgCl_2$ (0.5), and Tween 80 (0.5 mL/L). Anaerobic conditions were established by flushing with CO_2 for 20 min prior to sterilization (107°C, 50 min). Samples were serially diluted and incubated at 37°C for 72 h under anaerobic conditions on selective TPY agar (Rada and Koc, 2000) supplemented with mupirocin (100 mg/L) and glacial acetic acid (1 mL/L). Petri dishes were incubated in anaerobic jar (Oxoid, 3.5L) under carbon dioxide atmosphere generated by Oxoid CO_2 Gen Sachet ANA1044 (Thermo Scientific™).

Individual colonies were randomly selected and subcultured in anaerobic TPY broth. Purity and bifidobacterial morphology were confirmed microscopically. The same protocol was applied for the isolation of bifidobacteria from commercial probiotic and synbiotic products, except that 100 mg of lyophilized material was used. All isolates were stored at -80°C in TPY broth supplemented with glycerol (20%, v/v) until further use.

Molecular Identification of Isolates

The 16S rRNA gene was amplified using primers fD1 and rP2 (Engevik et al. 2021; Killer et al. 2014). Amplicons were sequenced bidirectionally using Sanger sequencing (Seqme, Czech Republic). The resulting sequences were assembled, aligned, and deposited in the NCBI database under the accession numbers listed in Table S1. Taxonomic assignment was based on 16S rRNA gene sequence similarity using the EzBioCloud database (Chalita et al. 2024). All isolates showed ≥ 99.6% sequence identity to their closest type strains.

Antidepressant Preparation and Growth Inhibition Assay

Three commonly prescribed antidepressants representing different pharmacological classes were tested for their effect on the growth of axenic bacterial cultures, including Brintellix® (Vortioxetine, 20 mg/mL), Seropram® (Citalopram, 40 mg/mL, and Cipralex® (Escitalopram, 20 mg/mL), all medications produced by H. Lundbeck A/S Denmark (Table 1). Drugs were used in their commercially available liquid formulation to maintain pharmaceutical-grade accuracy and chemical stability.

Each drug was tested at final concentrations of 200, 400, and 600 µg/mL. Triplicate cultures were prepared for each bacterial strain at each drug concentration. Inoculated culture medium without

antidepressant was used as a control for all strains. The volumes of medium and antidepressant stock solution for each condition are summarized in Table 2.

Table 2
Volumes of antidepressant and TPY medium for each final drug concentration.

Final concentration (µg/mL)	Volume of stock solution (mL) Brintellix and Cipralex (20 mg/mL)	Corresponding volume of TPY medium (mL)	Volume of stock solution (mL) Seropram (40 mg/mL)	Corresponding volume of TPY medium (mL)
0 (Control)	0	9.5	0	9.5
200	0.1	9.4	0.05	9.45
400	0.2	9.3	0.1	9.4
600	0.3	9.2	0.15	9.35

All cultures were incubated anaerobically at 37°C for 24 hours. Bacterial growth was monitored by measuring the optical density at 600 nm (OD_{600}) using a Thermo Spectronic Biomate 5 Spectrophotometer (Thermo Fisher Scientific, Wilmington, DE, USA). The initial OD_{600} values for all bacterial cultures, including both control and antidepressant-treated conditions, were approximately 0.2 at time zero. The change in OD_{600} served as an indicator of bacterial growth or inhibition.

Statistical Analysis

The optical density values (OD_{600}) measured after 24 hours of cultivation were used to assess the inhibitory effects of each antidepressant drug on bacterial growth. Statistical analyses and data visualization were conducted using RStudio (version 4.4.3). For each bacterial strain and antidepressant treatment, comparisons were performed between the control group and the different concentrations (200, 400, and 600 µg/mL) using the non-parametric Kruskal-Wallis test with the rstatix package with data manipulation done using the dplyr and tidyr packages. Percentage inhibition of bacterial growth was calculated from the optical density data. To compare the inhibitory effects of different antidepressant drugs at each concentration level, pairwise Wilcoxon rank-sum tests with Benjamini–Hochberg correction for multiple comparisons were performed. Only strain-drug combinations that showed statistically significant overall effects in the Kruskal-Wallis test ($p < 0.05$) were included in the analysis. For strain-drug combinations with significant effects, dose-response relationships were characterized by estimating the half-maximal inhibitory concentration (IC_{50}) through linear interpolation between measured OD_{600} values. To compare IC_{50} values across antidepressants, the Kruskal–Wallis test followed by pairwise Wilcoxon rank-sum tests with Benjamini–Hochberg correction for multiple comparisons were applied. Visualizations, including dose-response curves, bar plots, IC_{50} heatmaps, and boxplots comparing OD_{600} between strains, were created using the ggplot2 package.

Results

Antibacterial Activity of Antidepressants

The three tested antidepressants showed variable antibacterial activity against the 22 strains examined. Brintellix exhibited the strongest inhibitory effect, reducing bacterial growth across all strains, while Seropram showed the weakest activity, with limited growth inhibition. To quantify this inhibitory effect, the number of strains showing statistically significant differences ($p < 0.05$) between the control and increasing drug concentrations was assessed. Figure 1 shows that Brintellix affected the highest number of strains inhibiting 21 strains at 200 µg/mL, and 22 strains at both 400 and 600 µg/mL. Cipralex induced moderate inhibition, affecting 13 strains at 200 µg/mL and 16 strains at the higher doses (400 and 600 µg/mL). In contrast, Seropram showed the least impact, with 12 strains significantly inhibited at 200 µg/mL and 14 strains at 400 and 600 µg/mL.

Responses of individual bacterial strains to increasing concentrations of three antidepressants are showen by the curves in Fig. 2. Growth inhibitions were dependent both on the amount (0 to 600 µg/mL) and the type of drug. A progressive decline in OD_{600} values was observed for Brintellix in 21 tested strains, only strain *B. longum* subsp. *infantis* 2SY/TP4 was resistant to 200 µg/mL of Brintellix. Six strains were resistant to all three used concentrations of Cipralex, three strains still grew well at concentration 200 µg/mL, and 16 strains were progressively inhibited by higher amounts of Cipralex (400 and 600 µg/mL). The growth of eight bifidobacterial strains was not affected by Seropram, five strains grew well at concentration of 200 µg/mL, and 14 strains were suppressed by increased amounts of Seropram (400 and 600 µg/mL). Bacterial strains resistant to Cipralex and/or Seropram are shown in Fig. 3. Detailed results for each strain, including Kruskal-Wallis comparisons of control versus increasing antidepressant concentrations are available in Supplementary Table S2.

To further quantify the inhibitory effects, the percentage inhibition of bacterial growth at each tested concentration was calculated for all strain-drug combinations showing significant effects (Table S3). Brintellix showed the strongest inhibitory effect, reducing bacterial growth in almost all strains, reaching up to 72.7 ± 5.1% inhibition at 600 µg/mL, followed by Cipralex with 58.4 ± 5.4%, and Seropram with the weakest activity at 58 ± 4.1%. Mean percentage inhibition values by antidepressant and concentration are summarized in Table 3. Pairwise Wilcoxon rank-sum tests with Benjamini–Hochberg correction revealed that Brintellix had significantly higher percentage inhibition than Cipralex and Seropram at all concentrations ($p < 0.05$). No statistically significant differences were observed between Cipralex and Seropram at any concentration (Table S4).

Table 3
Mean percentage inhibition values ± SD induced by antidepressant at different concentrations.

Antidepressant	Concentration (µg/mL)	Mean inhibition ± SD (%)
Brintellix	200	28.7 ± 8.4
Brintellix	400	52.6 ± 5.5
Brintellix	600	72.7 ± 5.1
Cipralex	200	16.4 ± 8
Cipralex	400	35.6 ± 8.3
Cipralex	600	58.4 ± 5.4
Seropram	200	14.2 ± 8
Seropram	400	35.4 ± 7.7
Seropram	600	58 ± 4.1

IC_{50} analysis

The half-maximal inhibitory concentrations (IC_{50}) were calculated using linear interpolation to compare the inhibitory effects of each antidepressant on bifidobacterial strains. The IC_{50} values represent the concentration required to reduce bacterial growth by 50% and thus provide a comparative measure of drug effect. Brintellix displayed the lowest IC_{50} values for most sensitive strains, including *B. bifidum* CR2/5/TPMF2, CR3/BHMF/6, and CCM 3762. Across all tested strains, Brintellix yielded a mean IC_{50} of 379 µg/mL, indicating a higher overall inhibitory potential compared with the other antidepressants. In contrast, Cipralex and Seropram showed higher IC_{50} values, generally ranging between 400–590 µg/mL, which reflects weaker antibacterial activity. Statistical analysis using the Wilcoxon rank-sum test with Benjamini-Hochberg correction confirmed that Brintellix had significantly lower IC_{50} values than both Cipralex ($p = 2.36 \times 10^{-11}$) and Seropram ($p = 4.99 \times 10^{-9}$), while the difference between Cipralex and Seropram was not significant ($p = 0.941$). These findings are visualized in the IC_{50} heatmap (Fig. 4), with the full list of IC_{50} values for significantly affected strains provided in Supplementary Table S5.

Discussion

This study evaluated the *in vitro* antimicrobial activity of three commonly prescribed antidepressants, Brintellix, Cipralex, and Seropram, on 22 commensal strains of the *Bifidobacterium* genus.

The package leaflets for all three drugs list diarrhoea, constipation, dizziness, nausea, and indigestion as common or very common possible side effects. These warnings indicate that the aforementioned medicines affect the intestinal microbiome. This is supported by studies showing the influence of

antidepressant agents on both main gut bacterial phyla *Bacillota* and *Bacteroidota*(Shen et al. 2021; Borgiani et al. 2024). Literature data indicate a decrease of some beneficial genera, such as *Ruminococcus* and *Lachnospira* (Lin et al. 2025), or the decrease of *Lactobacillus*, and an increase of harmful *Fusobacterium*(Shen et al. 2021) due to the vortioxetine treatment. On the other hand, Shen et al. (2021) reported an increase of beneficial *Christensenellaceae* R-7 group, and *Eubacterium ruminantium* group after escilopram administration and Ye et al.(Ye et al. 2021) observed a higher abundance of *Akkermansia* due to vortioxetine treatment. It is evident that the results are not consistent and depend on the type of drug, illness severity and experimental design. However, gut microbiota profiles can be used as an effective appraisal to evaluate the therapeutic effect of antidepressants. The impact of ADs on beneficial gut microbes is therefore highly important.

Bifidobacteria are known as beneficial microbes used as probiotic bacterial strains, mainly for protecting against intestinal problems (Lim and Shin 2020). Given the possible side effects of antidepressants, the use of such supportive treatment is recommended.

Bifidobacteria are Gram-positive bacteria of phylum *Actinomycetota* colonizing the human gut. Their relative abundance in healthy individuals ranges between 2–14% and the incidence depends on many factors, including age, diet, genetic predisposition, birth mode, and health status (Hidalgo-Cantabrana et al., 2017). Their positive association with health and well-being is known and various intestinal, metabolic, and immune diseases cause their reduction or disappearance (Derrien et al., 2022). The beneficial impact of bifidobacteria is associated with producing lactic and acetic acid, strengthening the gut barrier function and modulating the immune system, which leads to antibacterial, antiviral, and anti-inflammatory effects (Lim and Shin, 2020). Bacteria of the same species as those used in our study are known for their health benefits and are often used as probiotics. *B. bifidum*, *B. adolescentis*, *B. longum*, *B. animalis*, *B. breve* have an influence on gut health by improving intestinal barrier integrity and boosting the immune system. Specific effects include alleviating symptoms of irritable bowel syndrome (IBS), constipation, and reducing allergic skin and respiratory inflammation (Zhang et al. 2019; Turroni et al. 2019; Yao et al. 2021; Cheng et al. 2021; Bocchio et al. 2024). *B. dentium* may contribute to dental caries due to the production of acid from saccharides, but on the other hand, it is also known to support gut health and reduce inflammation. Unlike other bifidobacterial species it does not degrade mucin glycans (Engevik et al. 2019). *B. crudilactis* is a species isolated from raw milk and raw milk cheeses (Delcenserie et al. 2007). Its antimicrobial activity and production of beneficial enzymes have prompted research into its use as a probiotic, but its specific health benefits are still being investigated. The recent study by Bocchio et al. (2024) provides a comprehensive overview of *Bifidobacterium*-based probiotics, highlighting their therapeutic impact on human diseases, including gastrointestinal, metabolic, and neurological conditions. This review emphasizes that different bifidobacterial species vary in their metabolic activities and health benefits, supporting their use as targeted probiotics for specific health outcomes.

Many of the above-mentioned species have recently attracted interest because of their potential positive impact on mood, mental health and neurodevelopmental disorders. The metabolic activities of *B. bifidum*

(Wang et al. 2022), B. *adolescentis* (Guo et al. 2019; Leser & Baker 2023), *B. longum* (Wang et al. 2019), B. *breve* (Li et al. 2022; Abdelhamid et al. 2025)d *dentium*(Engevik et al. 2021) are associated with gut-microbiota-brain axis function, production of neurotransmitters, modulation of the serotonergic system, and positive impacts on mood and cognitive function.

Recent research also shows the therapeutic potential of bifidobacteria in patients with depressive disorders (Nikolova et al. 2021). Their antidepressant effects might be related to anti-inflammatory effects and regulation of tryptophan metabolism, and 5-hydroxytryptamine synthesis (Li et al. 2023). *Bifidobacterium*-related probiotics are believed to have a positive impact on the treatment of depression (Morán et al. 2025). However, the potential of probiotics for treating mood disorders requires deeper, well-targeted research to clarify the mechanisms of drug action, the timing and dosing of treatment, and their association with the severity of depression (Merkouris et al. 2024).

The influence of antidepressants on the growth of axenic bacterial cultures has an important role in this research and presents a challenge for microbiologists working on the human gut microbiome. This research is particularly important, especially because our results indicate some individual responses of bifidobacterial strains to the tested antidepressants. SSRI antidepressants seem to be tolerated much better than SMS type. The tested strains were very sensitive to Brintellix. None of the strains were resistant to all used concentrations, and only the probiotic strain *B. longum*, subsp. *infantis* 11SY/TP2 grew in the presence of 200 µg/mL of Brintellix. On the other hand, eight bifidobacterial strains were resistant to all concentrations of Seropram, and moreover, two probiotic strains, *B. longum*, subsp. *infantis* 11SY/TP2 and 2SY/TP4, were resistant to the lowest concentration (200 µg/mL) of this drug. Six strains resistant to Seropram were also not susceptible to any concentration of Cipralex, and three additional strains tolerated its lowest concentration, two of them are used as probiotics (*B. longum*, subsp. *infantis* 11SY/TP2 and 2SY/TP4). Strains, that were resistant to all three concentrations of both antidepressants (Seropram and Cipralex) belonged to the *B. bifidum* species (four strains), *B. dentium* (one strain) and *B. longum* (one strain) Our preliminary data thus suggest that probiotics intended to support the treatment of depression should be specifically selected and tested for sensitivity to the drugs used in order to be meaningful.

From a clinical perspective, our findings suggest that antidepressants may have a direct influence on gut microbial composition through antimicrobial activity against key anaerobic commensals. The consistently stronger inhibition observed for Brintellix indicates that antidepressant class may be relevant not only for neuropsychiatric outcomes but also for gastrointestinal tolerance and microbiota stability. In patients receiving long-term antidepressant therapy, especially those suffering from gastrointestinal side effects or using probiotic supplementation, direct inhibition of bifidobacteria could contribute to altered gut function and variability in treatment response. These results demonstrate the clinical relevance of considering drug-microbiota interactions when selecting antidepressant regimens and designing adjunctive probiotic strategies.

Studies on the effect of AD on gut bacteria are still scarce, and the results are not unambiguous. *In vitro* study by (Rukavishnikov et al. 2023) compared the growth-inhibitory effects of SSRIs and SNRIs AD showing that fluvoxamine and venlafaxine exhibited weak effects on bacterial growth, while fluoxetine showed a strong inhibitory effect on the growth activity of *E. coli*, *E. feacalis*, *S. aureus*. Additionally, Cipralex had a marked effect on the growth rate of *E. coli*, *E. feacalis*, *B. bifidum*, *L. rhamnosus*, and *C. albicans*, while Mirtazapine showed the greatest activity against *L. rhamnosus* and *C. albicans*. However, other studies have reported only minor antimicrobial effects of Cipralex, with many strains exhibiting resistance (Kalaycı et al. 2015; Misera et al. 2023). This is in agreement with our results showing both types of response (resistance/sensitivity) to Cipralex for bifidobacterial strains.

Beyond the short-term effects detected *in vitro*, the long-term dynamics of microbial responses to antidepressant exposure, such as adaptation or reduced sensitivity are still not defined. A recent multi-omics human longitudinal cohort study found that antidepressant treatment had a weak inhibitory effect on the gut microbiota, leading to a reduction in microbial richness and functions (Wang et al. 2023). A review also indicates that antidepressants can alter gut microbiota composition (Sjöstedt et al. 2021; Ye et al. 2021). However, it is unclear if the gut microbiota adapts over time to sustain antidepressant exposure. Observational evidence shows that past medication use, including antidepressants, is associated with distinct gut microbiome features, even years later (Dilmore et al. 2025). Overall, the available literature does not provide evidence that bifidobacterial strains develop reduced sensitivity to antidepressants after prolonged exposure. This gap limits interpretation of how antidepressant medications interact with probiotic use and long-term gut microbiota stability.

One limitation of this study is its *in vitro* nature, which does not allow precise determination of the concentrations of antidepressants reaching the gastrointestinal tract *in vivo*. Factors such as dosage, absorption, and distribution affect drug levels in the gut. Tested antidepressant concentrations were selected to reflect physiologically relevant ranges in the human colon while accounting for variability in luminal fluid volumes. After a meal, the human colon contains around 2–97 mL of luminal fluid, resulting in wide inter-individual variations (Schiller et al., 2005; Murray et al., 2017). Calculations based on typical oral doses and estimated fractions reaching the colon(Sangkuhl et al., 2011; Carandang et al., 2011; Mahayni et al., 2013) indicate that local drug concentrations could vary widely depending on individual colonic fluid volume. The antidepressant concentration range tested in this study (200–600 µg/mL) reflects realistic exposure under average fluid conditions(Murray et al. 2017) and aligns with concentrations commonly used in *in vitro* studies (50–1000 µg/mL) for assessing microbiota modulation (Karine de Sousa et al. 2018; Ait Chait et al. 2020; Rukavishnikov et al. 2023). Typically, higher *in vitro* dosages are used than those expected *in vivo*(Handali & Rezaei 2020) to ensure measurable effects.

In conclusion, our findings demonstrated that antidepressants possess varying degrees of antimicrobial activity against bacteria of the genus *Bifidobacterium*. Brintellix displayed the most pronounced inhibition, suggesting that SMS-class antidepressants may exert stronger impacts on the gut microbiota than SSRIs. Antidepressant effects on *Bifidobacterium* populations could have an important effect on

health status. However, our results should be considered preliminary and exploratory, reflecting the nature of a pilot study. Further detailed research is needed to clarify this topic and to evaluate the effective use of probiotics in the treatment of depression. We plan to expand the investigation to additional clinically relevant bacterial strains, a broader range of drug concentrations, and assessments of the impact on the full human gut microbiome.

Declarations

We hereby declare that this research paper is original, unaided work and that all sources have been fully acknowledged. This work has not been submitted to any other journal.

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Authors´contributions

K.O.F., J.M.: conceptualization; K.O.F., J.K. and T.M.M.: methodology; T.M.M., J.K., L.J., K.H. and H.S.: formal analysis; T.M.M.: data curation, T.M.M.: writing-original draft preparation; K.O.F., H.S. and T.M.M.: writing-review and editing; K.O.F.: supervision. All authors have read and approved the final manuscript.

Availability of data and materials

We are ready to share our data.

Ethics approval and consent to participate

This work did not involve any experiments with humans or animals. Informed consent was obtained from all participants prior to their participation."

Conflict of Interest

The authors declare that they have no competing interests.

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Table 1

Table 1 is available in the Supplementary Files section.

Figures

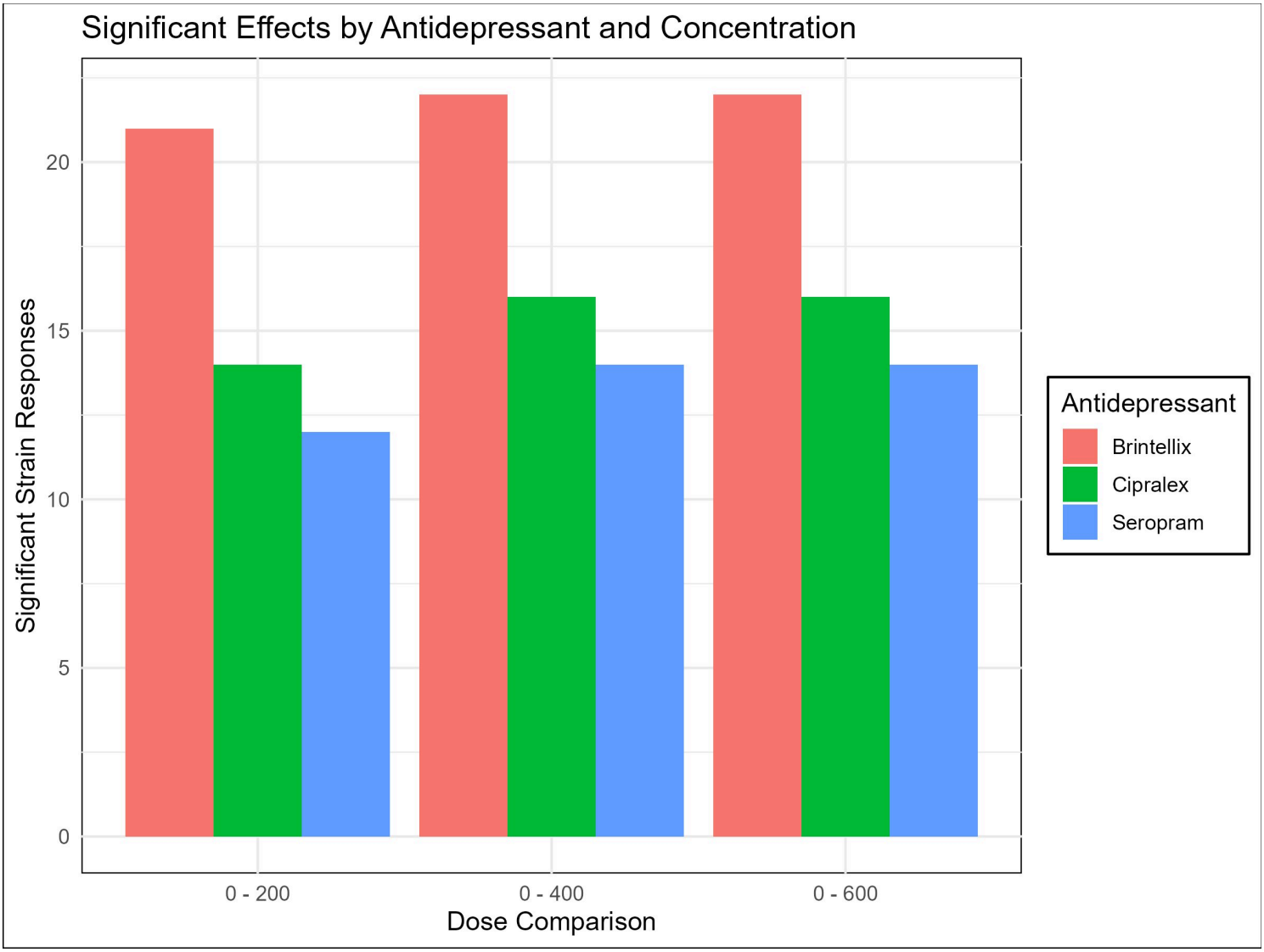


Figure 1

Barplot showing the number of bifidobacterial strains with significantly reduced growth in response to increasing concentrations (200, 400, and 600 µg/mL) of Brintellix, Cipralex, and Seropram. The X-axis represents the dose comparison for the three antidepressant medications tested. The Y-axis represents the number of strains that exhibited significantly reduced growth. The growth of each strain was evaluated at three concentrations (200, 400, and 600 µg/mL) and compared to the control (0 µg/mL) using a Kruskal–Wallis test. A strain was counted on the Y-axis if it showed a significant reduction in growth ($p < 0.05$) at any of the tested concentrations.

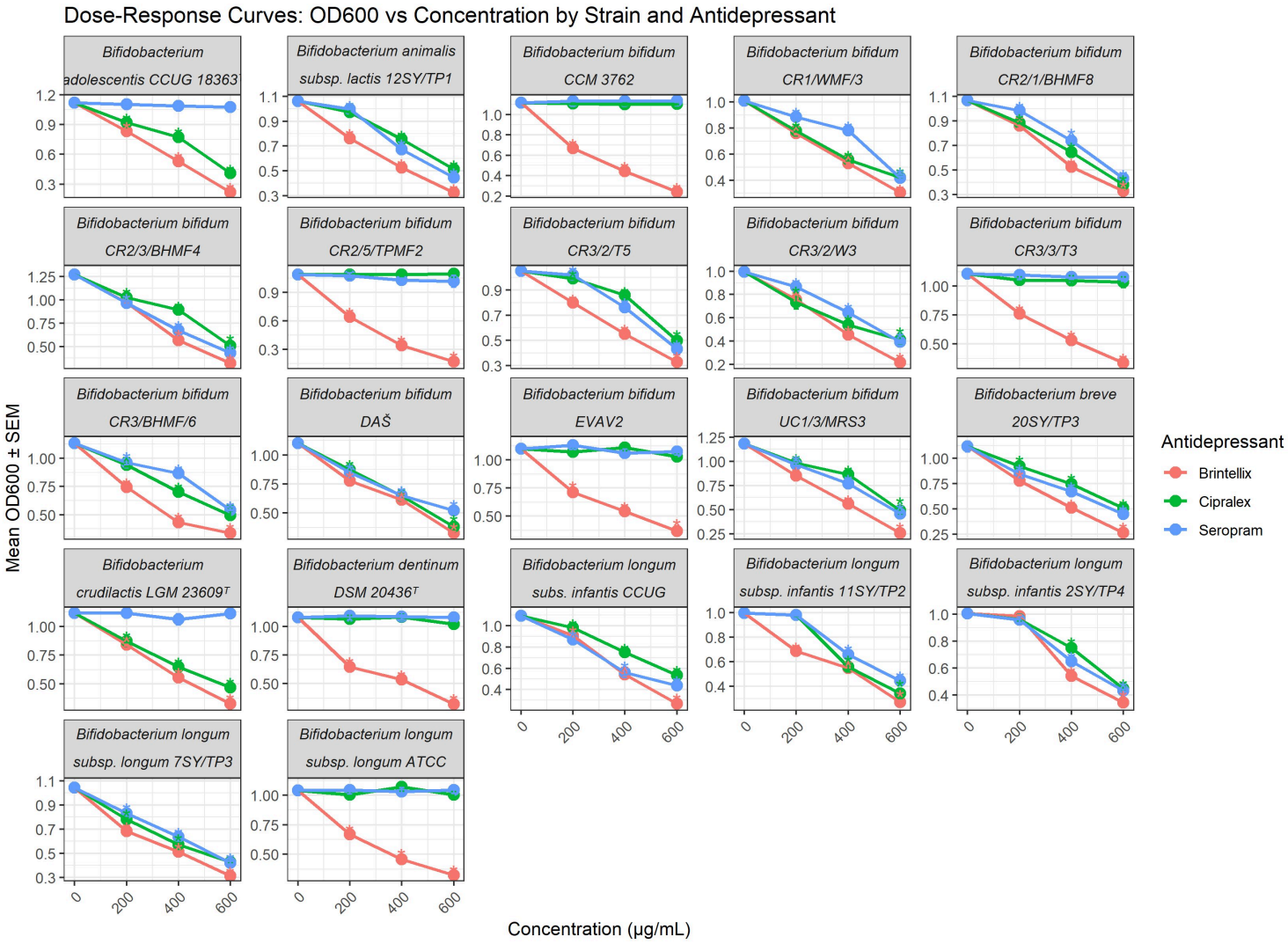


Figure 2

Growth inhibition curves of 22 bifidobacterial strains measured as OD_{600} with increasing concentrations (0–600 µg/mL) of the three antidepressants

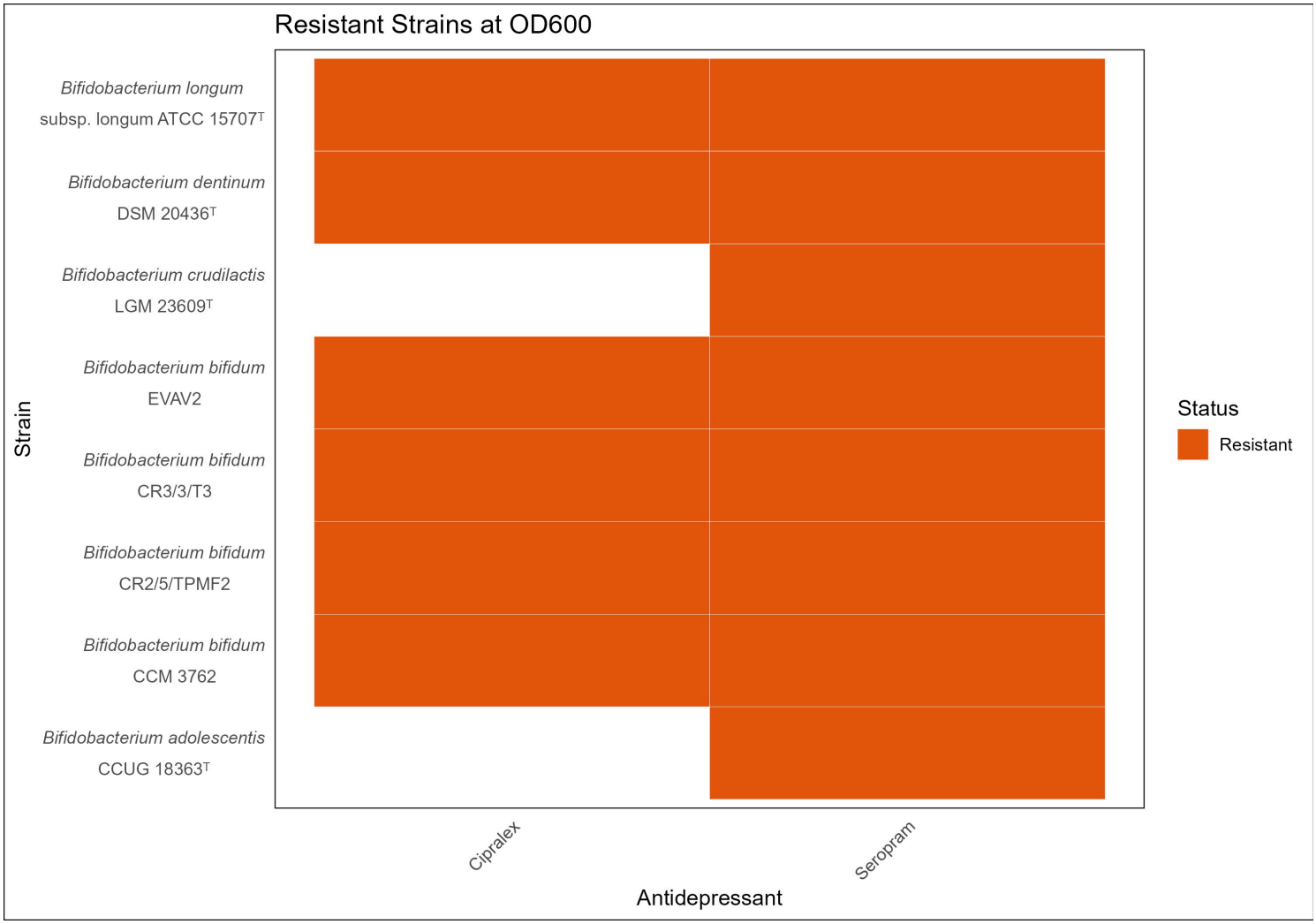


Figure 3

Tile plot displaying bifidobacterial strains identified as resistant ($p > 0.05$) to Cipralex and Seropram.

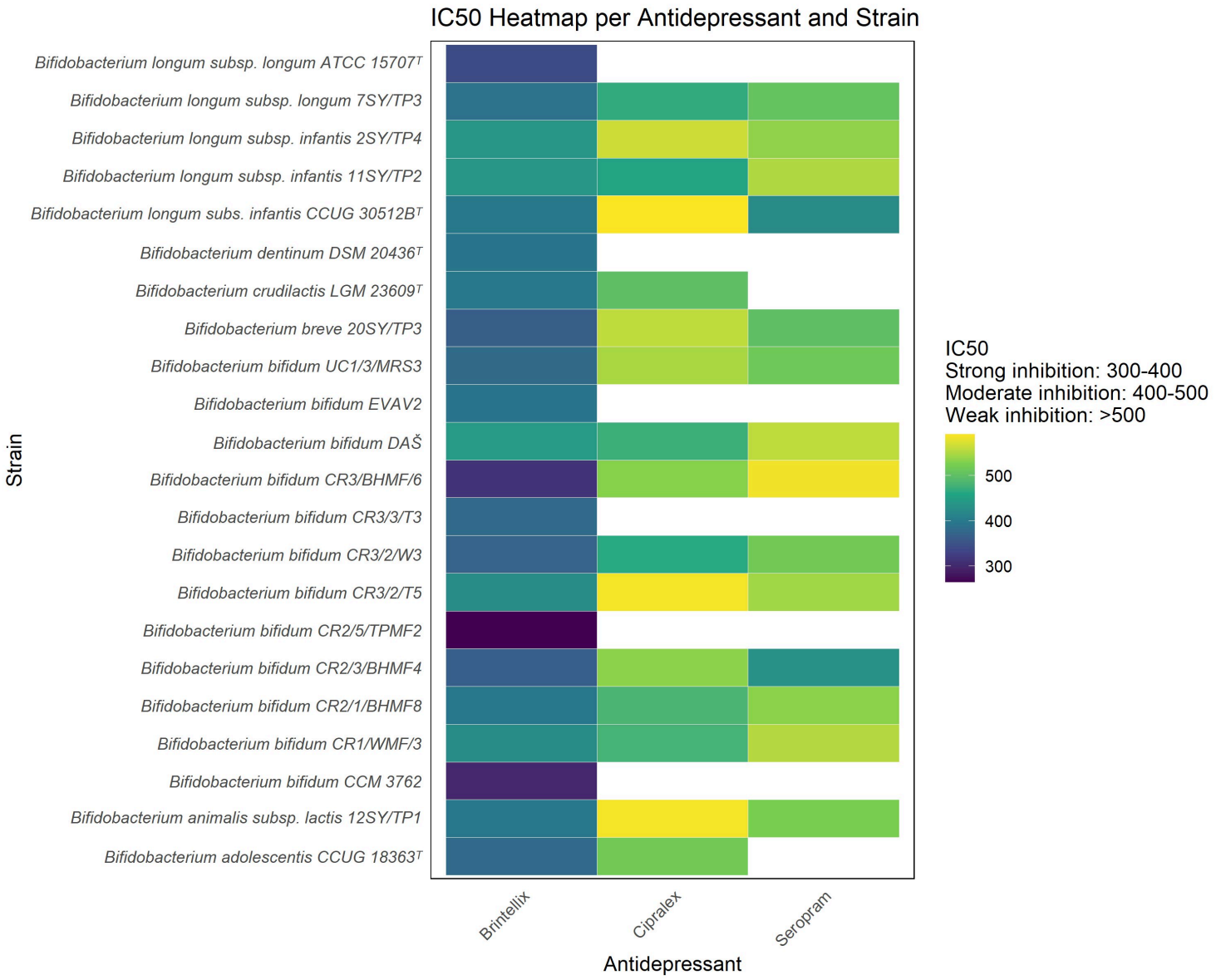


Figure 4

Heatmap of IC_{50} values (µg/mL) calculated by linear interpolation for each bifidobacterial strain exposed to Brintellix, Cipralex, and Seropram. The color scale represents antimicrobial effect, with darker shades indicating lower IC_{50} values (stronger inhibition).

Supplementary Files

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- Table1.docx