Supplementary file:

Unravelling the antimicrobial action of antidepressants on gut commensal microbes

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Table S1. Selected intestinal bacterial strains for the investigation of antibacterial activity.

Bacterial intestinal strains	**Culture medium**
Limosilactobacillus reuteri ATCC 23272	de Man Rogosa et Sharp (MRS)
Lacticaseibacillus casei ATCC 393	MRS
Lacticaseibacillus rhamnosus ATCC 53103	MRS
Bifidobacterium animalis subsp. animalis ATCC 25527	MRS
Enterococcus faecium ATCC 35667	MRS
Pseudomonas aeruginosa ATCC 27853	Brain Heart Infusion (BHI)
Escherichia coli ATCC 25922	BHI
Akkermansia muciniphila ATCC BAA-835	BHI + 0.5% mucin
Eubacterium rectale ATCC 33656	Fastidious Anaerobe Broth (FAB) + 0.5% yeast extract
Faecalibacterium prausnitzii ATCC 27768	FAB + 0.5% yeast extract
Bacteroides fragilis ATCC 25285	FAB + 0.5% yeast extract
Clostridium leptum ATCC 29065	FAB + 0.5% yeast extract

Table S2. Solvents used for psychotropics' stock solutions

Psychotropics	**Solvent**
Phenelzine	Water
Venlafaxine	Dimethylsulfoxide
(S)-Citalopram	Methanol
Desipramine	Water
Bupropion	Methanol
Aripiprazole	Acetic acid

Table S3. Inhibition zones diameters (mm) of some psychotropics against bacterial strains

Psychotropic / Strain	Desipramine			Aripiprazole			Phenelzine			(S)-Citalopram		
Concentration (mg/ml)	**10**	**5**	**2.5**	**10**	**5**	**2.5**	**10**	**5**	**2.5**	**10**	**5**	**2.5**
L. rhamnosus ATCC 53103	13 ± 0.22	10 ± 0.12	NI	24 ± 0.10	9 ± 0.11	NI	13 ± 0.12	NI	NI	9 ± 0.10	NI	NI
B. animalis ATCC 25527	25 ± 0.12	18 ± 0.20	NI	19 ± 0.11	9 ± 0.11	NI	12 ± 0.22	NI	NI	NI	NI	NI
E. faecium ATCC 35667	14 ± 0.21	11 ± 0.21	9 ± 0.10	17 ± 0.12	12 ± 0.21	9 ± 0.11	22 ± 0.21	17 ± 0.12	9 ± 0.14	14 ± 0.11	10 ± 0.12	NI
E. rectale ATCC 33656	21 ± 0.13	16 ± 0.11	10 ± 0.12	18 ± 0.12	13 ± 0.11	11 ± 0.21	12 ± 0.11	14 ± 0.10	9 ± 0.12	11 ± 0.12	NI	NI
F. prausnitzii ATCC 27768	22 ± 0.21	18 ± 0.11	15 ± 0.21	21 ± 0.10	17 ± 0.22	14 ± 0.11	20 ± 0.14	16 ± 0.11	13 ± 0.11	13 ± 0.11	9± 0.11	NI
B. fragilis ATCC 25285	20 ± 0.22	17 ± 0.20	14 ± 0.11	19 ± 0.11	15 ± 0.12	12 ± 0.12	13 ± 0.21	9 ± 0.10	NI	12 ± 0.21	9 ± 0.13	NI
E. coli ATCC 25922	21 ± 0.12	18 ± 0.12	16 ± 0.12	15 ± 0.11	12 ± 0.12	9 ± 0.11	19 ± 0.20	14 ± 0.22	10 ± 0.22	16 ± 0.12	11 ± 0.21	9 ± 0.10
C. leptum ATCC 29065	35 ± 0.10	29 ± 0.11	22 ± 0.21	31 ± 0.12	22 ± 0.22	19 ± 0.21	17 ± 0.11	14 ± 0.21	9 ± 0.23	20 ± 0.11	15 ± 0.22	11 ± 0.11
A. muciniphila ATCC BAA-835	32 ± 0.20	27 ± 0.12	20 ± 0.23	30 ± 0.13	22 ± 0.21	18 ± 0.22	21 ± 0.12	13 ± 0.12	10 ± 0.11	18 ± 0.13	14 ± 0.14	9 ± 0.13

NI: no inhibition detected

Table S4. Approximate concentrations of antidepressants reaching the human colon.

Drugs	Preclinical/clinical (mg / day) (min – max)	% reaching the colon[1]	Concentrations reaching the colon (µg/mL)		Tested concentrations (µg/mL)
			Colon volume 1* (min-max)	Colon volume 2** (min – max)	
Phenelzine	45 – 75	21	727 - 1212	20-33	75-800
Venlafaxine	75 – 225	13	750 - 2250	20-61	75-800
(S)-Citalopram	20 – 60	10	154 - 462	16-188	75-800
Desipramine	25 – 300	30	577 - 6923	21-94	75-800
Bupropion	100 - 450	10	769 - 3462	11-34	75-800
Aripiprazole	10 – 30	55	423 - 1269	4-13	75-800

[1]source: https://www.drugbank.ca

*: Colon fluid volume = 18 mL, according to [41]

**: Colon volume = 480 mL, according to [42]

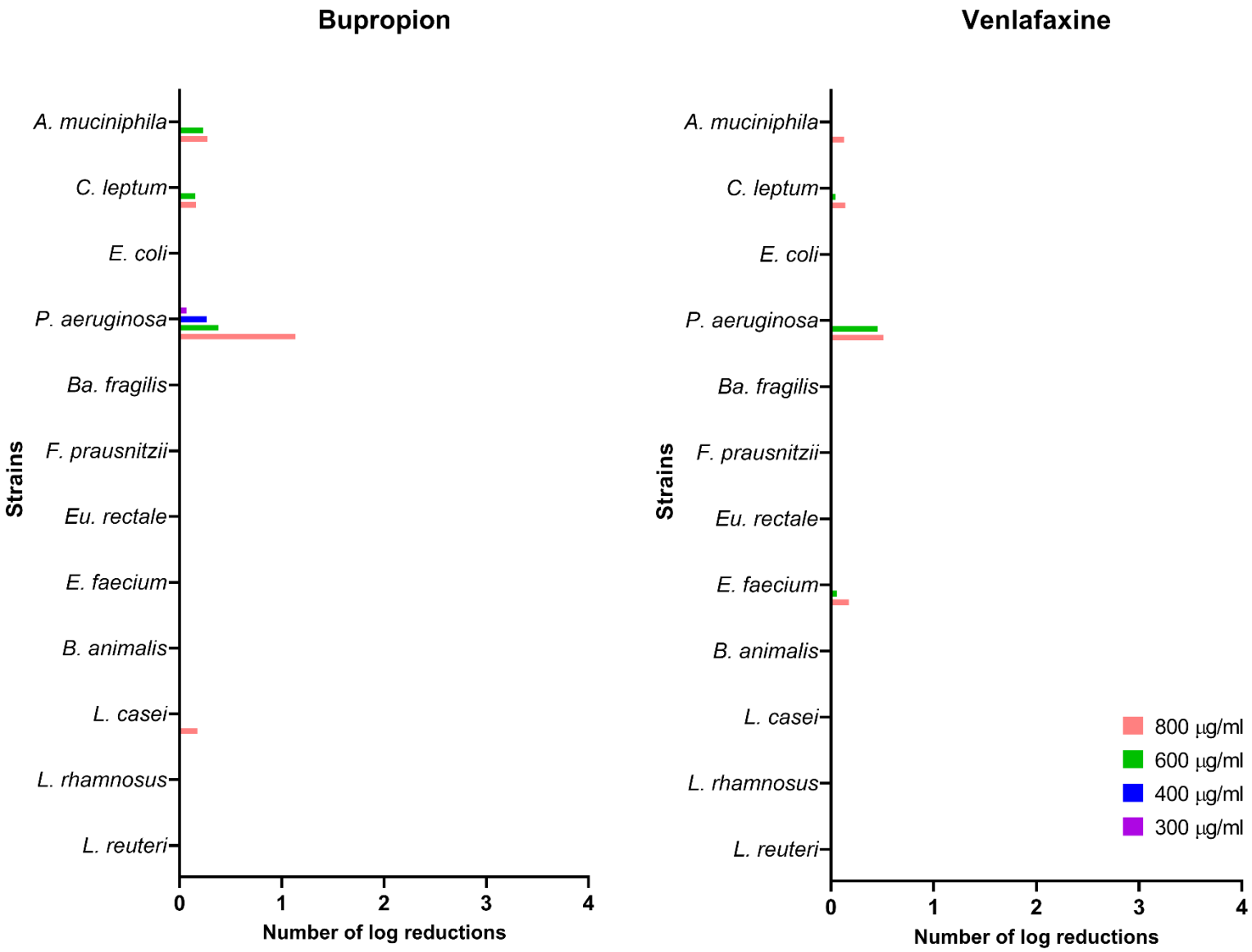

Figure S1. Logarithmic reductions of the growth of the commensal strains in the presence of bupropion and venlafaxine.

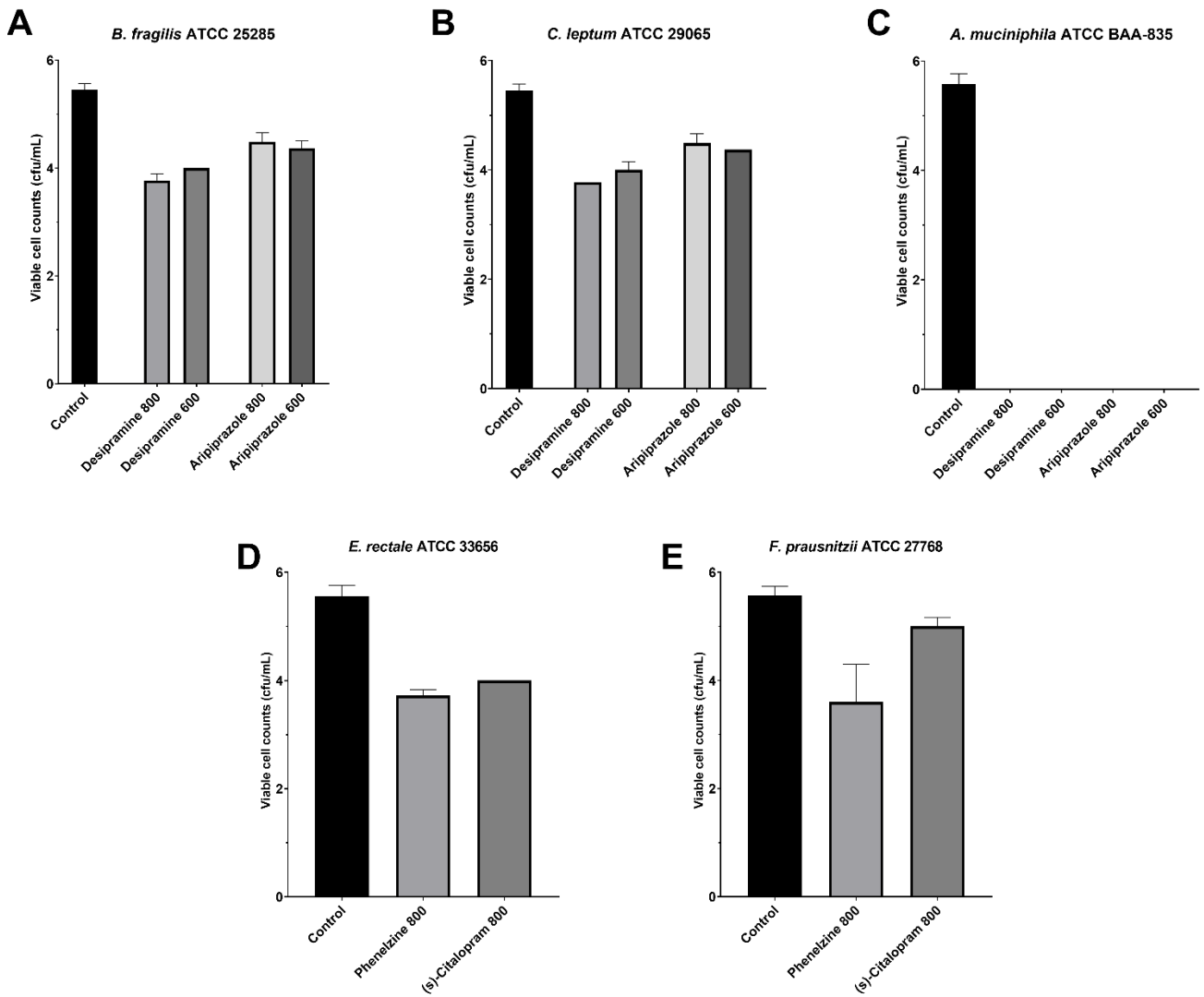

Figure S2. Bactericidal effect of desipramine, aripiprazole, phenelzine, and (s)-citalopram incubated for 16h at 600 and 800 µg/mL against tested bacterial strains. All treatments were statistically significant compared to control, which corresponds to initial inoculum cell counts (cfu/mL).

REFERENCES

41. Schiller, C. *et al.* Intestinal fluid volumes and transit of dosage forms as assessed by magnetic resonance imaging. *Aliment. Pharmacol. Ther.* **22**, 971–979 (2005).
42. Pritchard, S. E. *et al.* Fasting and postprandial volumes of the undisturbed colon: normal values and changes in diarrhea-predominant irritable bowel syndrome measured using serial MRI. *Neurogastroenterol. Motil.* **26**, 124–130 (2014).