

Impact of enniatin and deoxynivalenol co-occurrence on plant, microbial, insect, animal and human systems: current knowledge and future perspectives” by Irene Valenti ¹, Francesco Tini ^{2,*}, Milos Sevarika ², Alessandro Agazzi ³, Giovanni Beccari ², Ilaria Bellezza ⁴, Luisa Ederli ², Silvia Grottelli ⁴, Matias Pasquali ¹, Roberto Romani ², Marco Saracchi ², and Lorenzo Covarelli ²

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Supplementary Table S1: In vitro effects of ENNs on microorganisms.

* = not sensitivity at the highest test concentration; ^a = MIC value; ^b = IC₅₀ value.

	Species/Cell line	Sensitivity	ENN type	Reference
Bacteria	<i>Cryptococcus neoformans</i> ATCC 90113	12.5 µg/ml ^a	ENA	195
		12.5 µg/ml ^a	ENA1	
		25 µg/ml ^a	ENB1	
	<i>Clostridium perfringens</i> CECT 4647	0.2 µg ^a	ENB	122
	<i>Enterococcus faecium</i> CECT 410	2000 µg ^a		
	<i>Escherichia coli</i> CECT 4782	>2000 µg ^{a*}		
	<i>Listeria monocytogenes</i> CECT 935	2000 µg ^a		
	<i>Pseudomonas aeruginosa</i> CECT 4628	2000 µg ^a		
	<i>Salmonella enterica</i> CECT 554	200 µg ^a		
	<i>Shigella dysenteriae</i> CECT 584	>2000 µg ^{a*}		
	<i>Staphylococcus aureus</i> CECT 240	>2000 µg ^{a*}		
	<i>Staphylococcus aureus</i> CECT 976	0.2 µg ^a		
	<i>Yersinia enterocolitica</i> CECT 4054	2000 µg ^a		
	<i>Mycobacterium intracellulare</i> ATCC 23068	50 µg/ml ^a	ENA	195
		50 µg/ml ^a	ENA1	
		>50 µg/ml ^{a*}	ENB1	
	<i>Mycobacterium tuberculosis</i> H37Ra	3.12 µg/ml ^a	ENB	120
		3.12 µg/ml ^a	ENB4	
		6.25 µg/ml ^a	ENC	
		6.25 µg/ml ^a	ENG	
		6.25 µg/ml ^a	ENH	
		6.25 µg/ml ^a	ENI	

<i>Mycobacterium tuberculosis</i> H37Ra ATCC25177	2 µg/ml ^a	ENA1	119
<i>Mycobacterium tuberculosis</i> H37Rv ATCC27294	1 µg/ml ^a		
<i>Mycobacterium bovis</i> ATCC19210	2 µg/ml ^a		
<i>Mycobacterium bovis</i> BGC ATCC35737	2 µg/ml ^a		
<i>Mycobacterium smegmatis</i> mc ² 155	8 µg/ml ^a		
<i>Escherichia coli</i> ATCC25922	>100 µg/ml ^a		
<i>Klebsiella pneumonia</i> CTCC46117	>100 µg/ml ^a		
<i>Listeria monocytogenes</i> ATCC19115	>100 µg/ml ^a		
<i>Pseudomonas aeruginosa</i> ATCC9027	>100 µg/ml ^a		
<i>Staphylococcus aureus</i> ATCC75923	>100 µg/ml ^a		
<i>Bifidobacterium adolescentis</i> CECT 5781	>1000 ng ^{a*}	ENJ1	127
<i>Bifidobacterium bifidum</i> CECT 870T	10 ng ^a		
<i>Bifidobacterium breve</i> CECT 4839T	100 ng ^a		
<i>Bifidobacterium longum</i> CECT 4551	1000 ng ^a		
<i>Clostridium perfringens</i> CECT 4647	100 ng ^a		
<i>Enterococcus faecium</i> CECT 410	10 ng ^a		
<i>Escherichia coli</i> CECT 4782	>1000 ng ^{a*}		
<i>Lactobacillus animalis</i> CECT 4060T	100 ng ^a		
<i>Lactobacillus casei</i> CECT 475	1000 ng ^a		
<i>Lactobacillus casei subsp. casei</i> CECT 475	1000 ng ^a		
<i>Lactobacillus casei rhamnosus</i> CECT 278T	10 ng ^a		
<i>Lactobacillus plantarum</i> CECT 220	10 ng ^a		
<i>Lactobacillus ruminis</i> CECT 4061T	1000 ng ^a		
<i>Listeria monocytogenes</i> CECT 935	>1000 ng ^{a*}		
<i>Pseudomonas aeruginosa</i> CECT 4628	>1000 ng ^{a*}		
<i>Salmonella enterica</i> CECT 554	>1000 ng ^{a*}		
<i>Shigella dysenteriae</i> CECT 584	100 ng ^a		
<i>Staphylococcus aureus</i> CECT 976	1000 ng ^a		
<i>Staphylococcus aureus</i> CECT 240	1000 ng ^a		
<i>Yersinia enterocolitica</i> CECT 4054	100 ng ^a		
<i>Bifidobacterium adolescentis</i> CECT 5781	1000 ng ^a	ENJ3	

	<i>Bifidobacterium bifidum</i> CECT 870T	10 ng ^a		
	<i>Bifidobacterium breve</i> CECT 4839T	>1000 ng ^{a*}		
	<i>Bifidobacterium longum</i> CECT 4551	10 ng ^a		
	<i>Clostridium perfringens</i> CECT 4647	1000 ng ^a		
	<i>Enterococcus faecium</i> CECT 410	1000 ng ^a		
	<i>Escherichia coli</i> CECT 4782	1000 ng ^a		
	<i>Lactobacillus animalis</i> CECT 4060T	10 ng ^a		
	<i>Lactobacillus casei</i> CECT 475	100 ng ^a		
	<i>Lactobacillus casei subsp. casei</i> CECT 475	1000 ng ^a		
	<i>Lactobacillus casei rhamnosus</i> CECT 278T	1000 ng ^a		
	<i>Lactobacillus plantarum</i> CECT 220	1000 ng ^a		
	<i>Lactobacillus ruminis</i> CECT 4061T	1000 ng ^a		
	<i>Listeria monocytogenes</i> CECT 935	>1000 ng ^{a*}		
	<i>Pseudomonas aeruginosa</i> CECT 4628	>1000 ng ^{a*}		
	<i>Salmonella enterica</i> CECT 554	>1000 ng ^{a*}		
	<i>Shigella dysenteriae</i> CECT 584	10 ng ^a		
	<i>Staphylococcus aureus</i> CECT 976	>1000 ng ^{a*}		
	<i>Staphylococcus aureus</i> CECT 240	10 ng ^a		
	<i>Yersinia enterocolitica</i> CECT 4054	>1000 ng ^{a*}		
	<i>Bifidobacterium adolescentis</i> 5871	>20,000 ng ^{a*}	ENA	101
		>20,000 ng ^{a*}	ENA1	
		>20,000 ng ^{a*}	ENA2	
		20 ng ^a	ENB1	
	<i>Bifidobacterium bifidum</i> 870T	>20,000 ng ^{a*}	ENA	
		20,000 ng ^a	ENA1	
		>20,000 ng ^{a*}	ENA2	
		20,000 ng ^a	ENB1	
	<i>Bifidobacterium breve</i> 4839T	>20,000 ng ^{a*}	ENA	
		20,000 ng ^a	ENA1	
		>20,000 ng ^{a*}	ENA2	
		>20,000 ng ^{a*}	ENB1	
	<i>Bifidobacterium longum</i> 4551	>20,000 ng ^{a*}	ENA	
		20,000 ng ^a	ENA1	

			>20,000 ng ^{a*}	ENA2	
			20,000 ng ^a	ENB1	
	<i>Lactobacillus casei</i> 4180		>20,000 ng ^{a*}	ENA	
			20,000 ng ^a	ENA1	
			>20,000 ng ^{a*}	ENA2	
			>20,000 ng ^{a*}	ENB1	
	<i>Lactobacillus casei- casei</i> 4180		>20,000 ng ^{a*}	ENA	
			20,000 ng ^a	ENA1	
			>20,000 ng ^{a*}	ENA2	
			20,000 ng ^a	ENB1	
	<i>Lactobacillus rhamnosus</i> 278T		>20,000 ng ^{a*}	ENA	
			20,000 ng ^a	ENA1	
			>20,000 ng ^{a*}	ENA2	
			>20,000 ng ^{a*}	ENB1	
	<i>Lactobacillus ruminis</i> 4061 T		>20,000 ng ^{a*}	ENA	
			20,000 ng ^a	ENA1	
			>20,000 ng ^{a*}	ENA2	
			20,000 ng ^a	ENB1	
	<i>Streptococcus thermophilus</i> 986		>20,000 ng ^{a*}	ENA	
			20,000 ng ^a	ENA1	
			>20,000 ng ^{a*}	ENA2	
			2,000 ng ^a	ENB1	
Protozoa	<i>Leishmania donovani</i> ATCC 39930D		10 µg/ml ^b	ENNs mix (A, A1, B, B1, B2 and Q)	118
	<i>Plasmodium falciparum</i> K1		0.27 µg/ml ^b	ENB	120
			0.20 µg/ml ^b	ENB4	
			1.1 µg/ml ^b	ENC	
			0.46 µg/ml ^b	ENG	
			1.9 µg/ml ^b	ENH	
			0.24 µg/ml ^b	ENI	
Fungi	Yeast	<i>Candida albicans</i> ATCC 90028	3.13 µg/ml ^a	ENA	195
			6.25 µg/ml ^a	ENA1	

		6.25 µg/ml ^a	ENB1	
	<i>Saccharomyces cerevisiae</i> 7	2000 ng ^a	ENA	101
		>20,000 ng ^{a*}	ENA1	
		>20,000 ng ^{a*}	ENA2	
		>20,000 ng ^{a*}	ENB1	
	<i>Saccharomyces cerevisiae</i> 15	>20,000 ng ^{a*}	ENA	
		>20,000 ng ^{a*}	ENA1	
		2000 ng ^a	ENA2	
		>20,000 ng ^{a*}	ENB1	
	<i>Aspergillus flavus</i> CECT 2684	>20 µg ^{a*}	ENB	100
	<i>Aspergillus flavus</i> CECT 2685	>20 µg ^{a*}		
	<i>Aspergillus fumigatus</i> CECT 20366	>20 µg ^{a*}		
	<i>Aspergillus ochraceus</i> CECT 2092	>20 µg ^{a*}		
	<i>Aspergillus parasiticus</i> CECT 2680	>20 µg ^{a*}		
	<i>Beauveria bassiana</i> CECT 20499	5 µg ^a		
	<i>Beauveria bassiana</i> CECT 20191	5 µg ^a		
	<i>Beauveria bassiana</i> CECT 20412	5 µg ^a		
	<i>Fusarium oxysporum</i> CECT 2715	>20 µg ^{a*}		
	<i>Fusarium poae</i> CECT 20165	>20 µg ^{a*}		
	<i>Fusarium proliferatum</i> CECT 20569	>20 µg ^{a*}		
	<i>Fusarium proliferatum</i> CECT 50546	>20 µg ^{a*}		
	<i>Fusarium sporotrichioides</i> CECT 20166	>20 µg ^{a*}		
	<i>Fusarium tricinctum</i> CECT 20150	>20 µg ^{a*}		
	<i>Fusarium verticilloides</i> CECT 2152	>20 µg ^{a*}		
	<i>Fusarium verticilloides</i> CECT 2982	>20 µg ^{a*}		
	<i>Fusarium verticilloides</i> CECT 2987	>20 µg ^{a*}		
	<i>Penicillium expansum</i> CECT 2275	>20 µg ^{a*}		
	<i>Penicillium expansum</i> CECT 2278	>20 µg ^{a*}		
	<i>Trichoderma harzianum</i> T22	1 µg ^a		
	<i>Fusarium avenaceum</i>	100 mg/kg ^a	ENB	65
	<i>Fusarium graminearum</i>	50 mg/kg ^a		
	<i>Aspergillus fumigatus</i> ATCC 90906	>50 µg/ml ^{a*}	ENA	195
		>50 µg/ml ^{a*}	ENA1	

	<i>Botrytis cinerea</i>	>50 µg/ml ^{a*}	ENB1	196
		>100 µg/ml ^a	ENB	
		75 µg/ml ^a	ENB1	
		>100 µg/ml ^a	ENB2	
		>100 µg/ml ^a	ENB4	
		>100 µg/ml ^a	ENJ1	
		>100 µg/ml ^a	ENJ4	

Supplementary Table S2: Effects of ENNs on insects.

* = not sensitivity at the highest test concentration; a = MIC value.

Species	Sensitivity	ENN type	Reference
<i>Aphis craccivora</i>	10 – 500 mg/L of <i>Cordyceps fumosorosea</i> micelial extract	ENK1	149
<i>Bemisia tabaci</i>	10 – 500 mg/L of <i>Cordyceps fumosorosea</i> micelial extract	ENK1	
<i>Tenebrio molitor</i>	> 14.26 µg/g ^a	Enniatin complex	150
<i>Galleria mellonella</i>	100 µg/g [*]	ENB	148
<i>Choristoneura fumiferana</i>	400 µg/g ^a	ENA/A ₁	147
<i>Aedes aegypti</i>	10-75 µg/ml ^a	ENA / Enniatin complex	146
<i>Calliphora erythrocephala</i>	5-10 µg/fly ^a	ENA / Enniatin complex	