

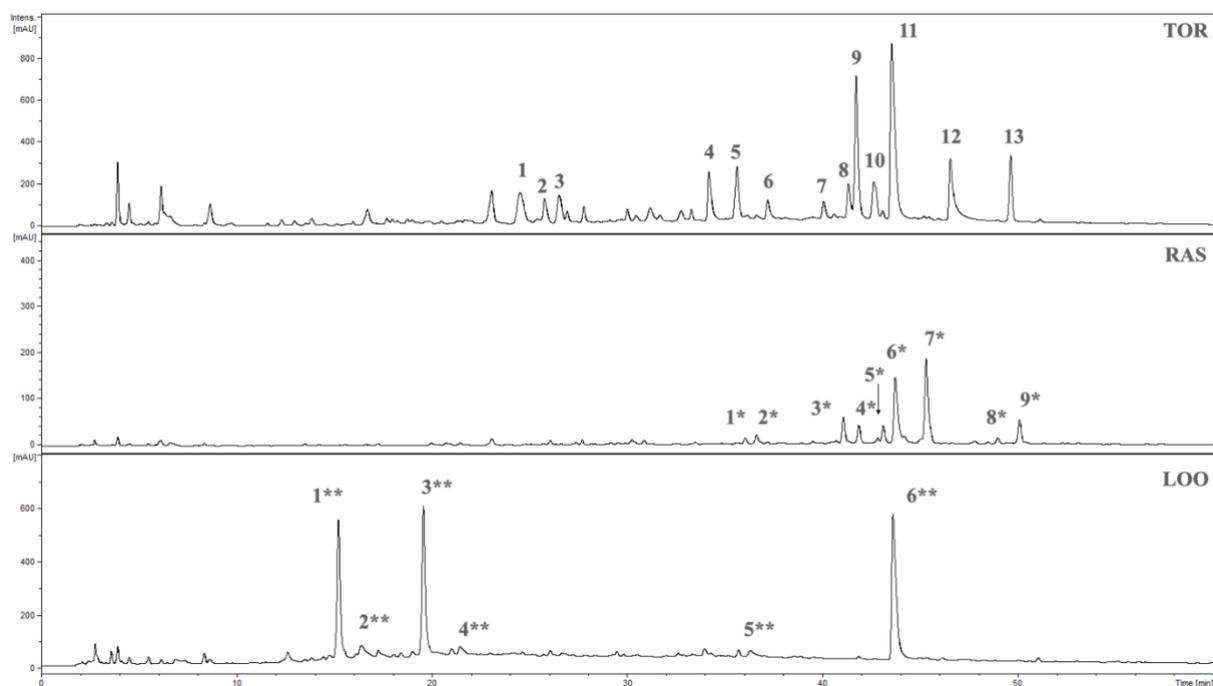
Therapeutic effects of oral application of menthol and extracts from tormentil (*Potentilla erecta*), raspberry leaves (*Rubus idaeus*), and loosestrife (*Lythrum salicaria*) during acute murine campylobacteriosis

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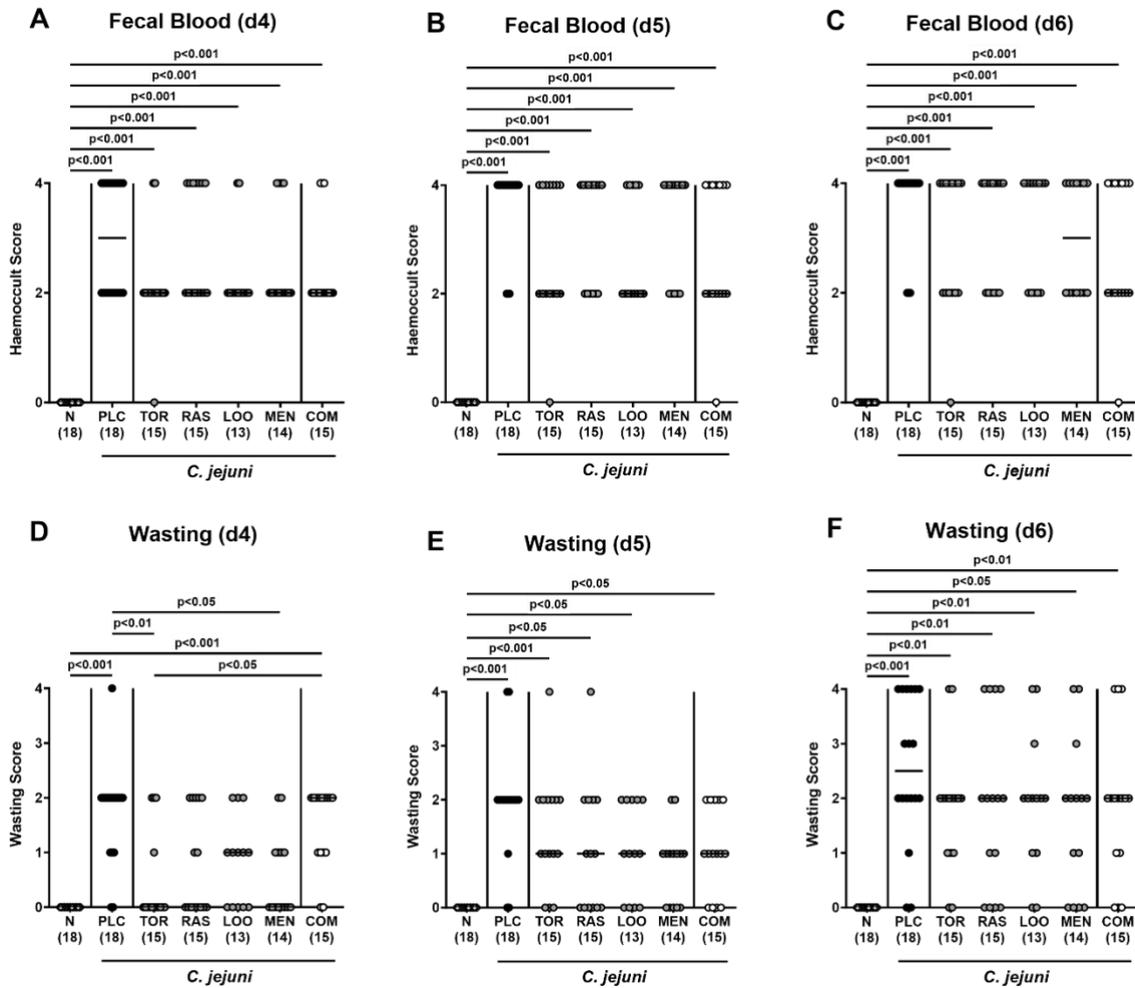
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Supplementary Figure S1: LC-DAD-IT-MS analysis of tormentil (TOR), raspberry leaves (RAS), and loosestrife (LOO) extracts. Peaks are labelled with the respective compound numbers according to the data displayed in Table S1.

Supplementary Table S1: Retention Times and MS² Data for tormentil (TOR), raspberry leaves (RAS), and loosestrife (LOO) extracts.

Extract	Number	Identification	retention time [min]	λ max (nm)	m/z [M – H] ⁻	MS ² ions	Reference
TOR	1	dimeric procyanidin B type	24.5	278	577	559, 451, 425b , 407, 289	10.1002/pca.2570
	2	catechin	25.8	278	289	245b, 205, 125	10.1002/pca.2570
	3	trimeric procyanidin C type	26.5	277	865	847, 739, 695b, 577, 425, 407, 287	10.1002/pca.2570
	4	pentameric procyanidin	34.6	279	1441	1153b, 863, 575, 289	10.1002/pca.2570
	5	tertameric procyanidin	36.3	279	1153	1027, 983, 865b, 863, 695	10.1002/pca.2570
	6	leavigatin 1, 2 or 3	37.3	268	1567	934b, 783, 633	10.1002/pca.2570
	7	gallic acid derivative	40.3	269	511	465b, 221	-
	8	leavigatin 1, 2 or 3	41.5	268	1567	934b, 783, 633	10.1002/pca.2570
	9	ellagic acid pentoside	41.9	251, 360	433	301b	10.1002/pca.2570
	10	methylellagic acid hexoside	42.7	250, 364	477	315b	10.1002/pca.2570
	11	ellagic acid	43.9	250, 367	301	230b	10.1002/pca.2570
	12	agrimoniin	46.7	268	1869	1567b, 1085	10.1002/pca.2570
	13	methylellagic acid pentoside	49.7	246, 364	447	315b, 300	10.1002/pca.2570
RAS	1*	phenolic acid derivative	36.2	255, 300, 324	339	321, 177b	-
	2*	sanguin H-10 isomer	36.8	268	1568	1235, 935, 783b, 301	10.3390/plants10112317
	3*	quercetin rhamnohexoside	41.2	255, 352	609	301b, 179	10.3390/plants10112317
	4*	quercetin pentoside	42.0	254, 351	433	301b	10.3390/plants10112317
	5*	ellagic acid pentoside	43.2	255, 360	433	301b, 191	10.3390/plants10112317
	6*	ellagic acid	43.8	252, 367	301	255b	10.3390/plants10112317
	7*	quercetin glucuronide	45.6	256, 352	477	301b, 227, 151	10.3390/plants10112317
	8*	quercetin derivative	48.6	254, 351	607	505, 463b, 301	10.3390/plants10112317
	9*	kaempferol glucuronide	50.2	264, 340	461	285b, 257	10.3390/plants10112317
LOO	1**	vescalagin	15.3	260	933	915b, 782, 570, 445, 301	10.1002/pca.2415
	2**	salicarinin A	16.5	259	1867	1083, 933b, 631, 301	10.1002/pca.2415
	3**	castalagin	19.3	260	933	915, 897, 631b, 441	10.1002/pca.2415
	4**	salicarinin B	21.7	260	1867	1547, 915b, 631, 301	10.1002/pca.2415
	5**	isoorientin	36.5	262, 351	447	429, 357, 327	10.1002/pca.2415
	6**	ellagic acid	43.8	252, 364	301	255b, 241	10.1002/pca.2415

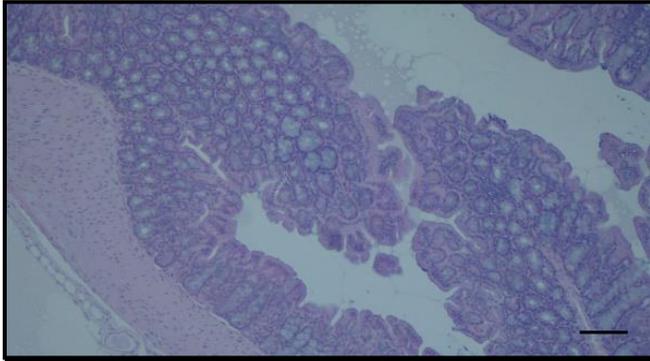


Supplementary Figure S2: Abundance of fecal blood and wasting symptoms over time following oral treatment of infected gut microbiota depleted IL-10^{-/-} mice with distinct natural compounds alone or in combination. Mice were orally infected with *C. jejuni* 81-176 strain on days 0 and 1. From day 2 until day 6, mice were treated with either tormentil (TOR), raspberry leaves (RAS), loosestrife (LOO), and menthol (MEN) alone or with a combination of all four compounds (COM) via the drinking water. Placebo control mice received vehicle only (PLC), whereas naive mice (N) served as uninfected and untreated controls. Severities of clinical campylobacteriosis signs such as (A-C) fecal blood and (D-F) wasting symptoms were determined at defined time points post-infection by clinical scoring schemes. Medians (black bars), significance levels (p values) determined by the Kruskal-Wallis test with Dunn's multiple comparison test, and numbers of mice included from three independent experiments (in parentheses) are indicated.

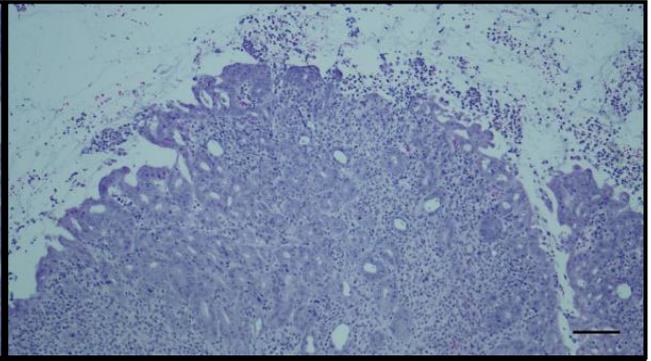
A

Histopathology - COLON

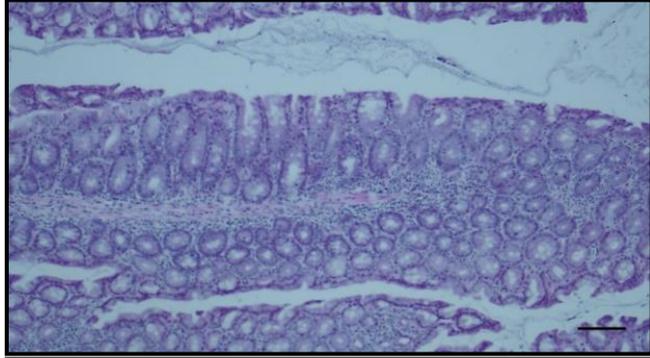
N



PLC



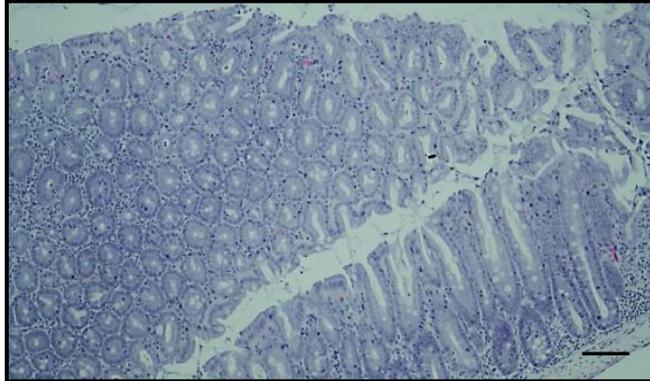
TOR



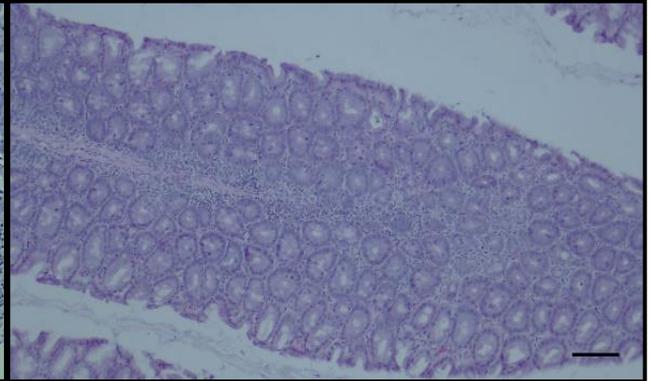
RAS



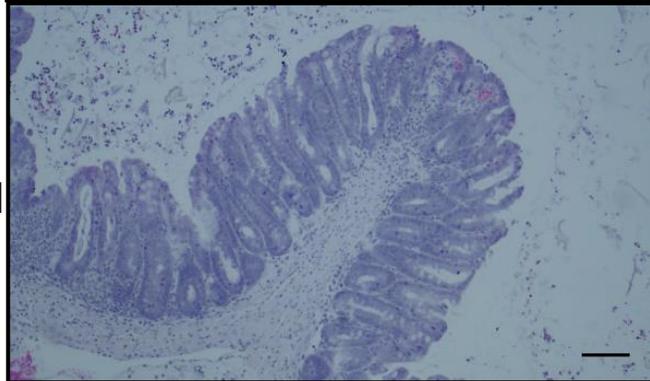
LOO



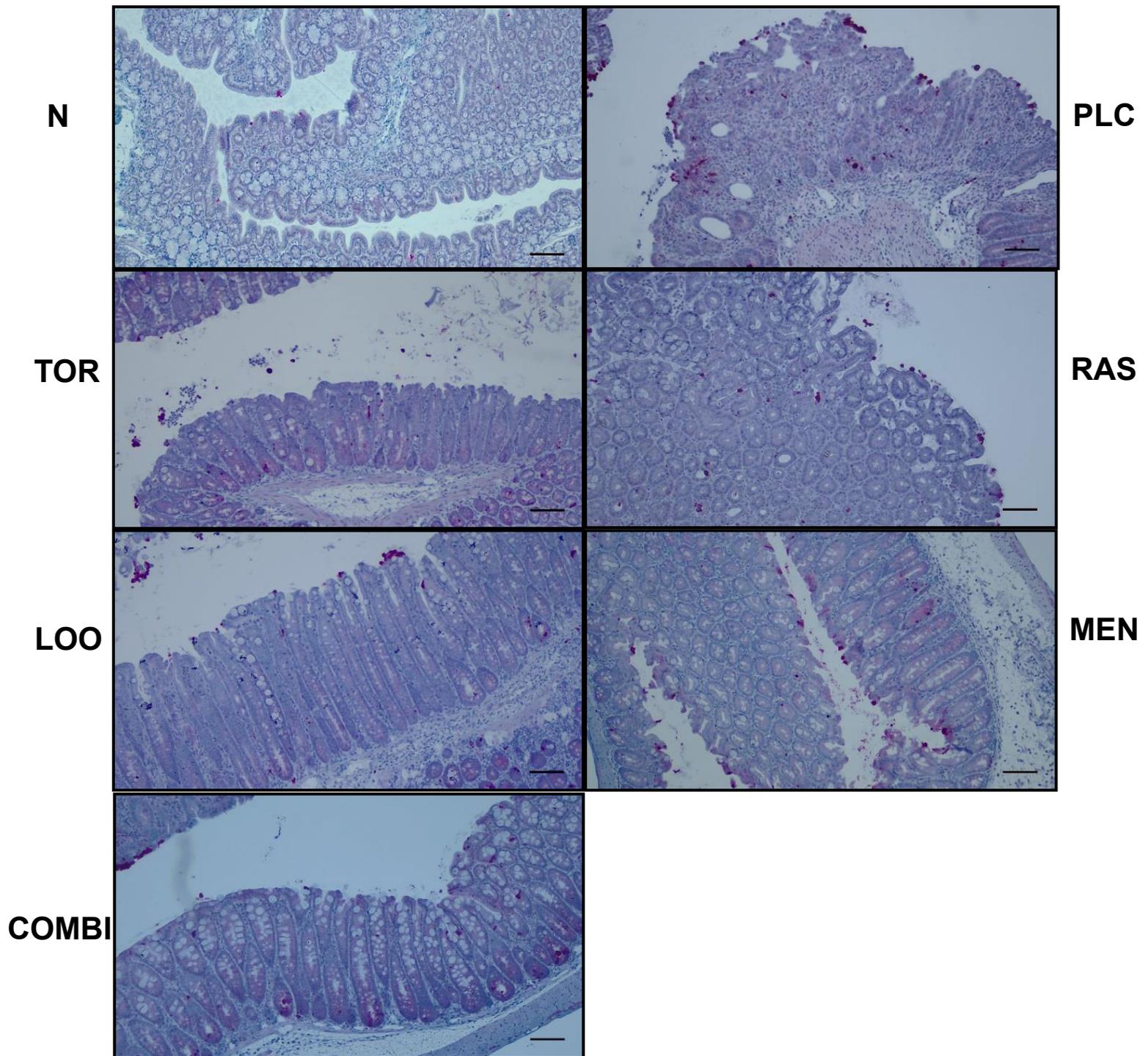
MEN



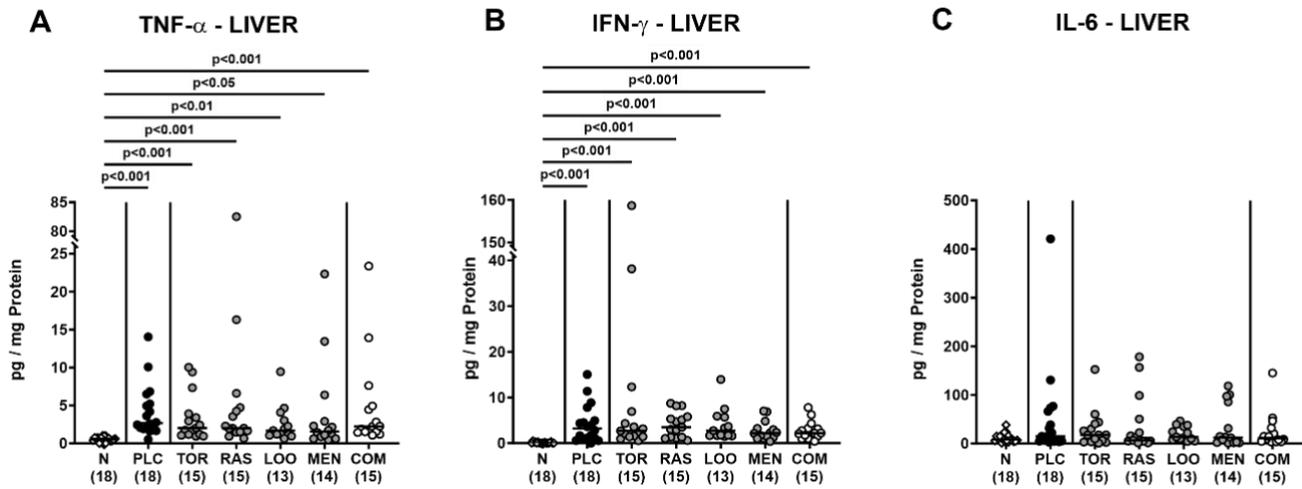
COMBI



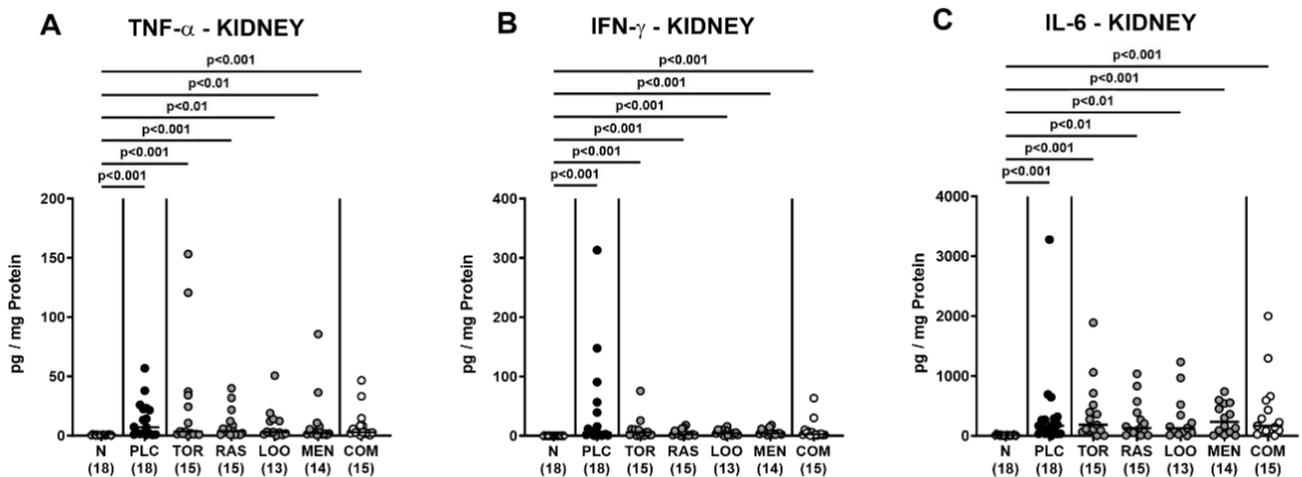
B Apoptotic Cells - COLON



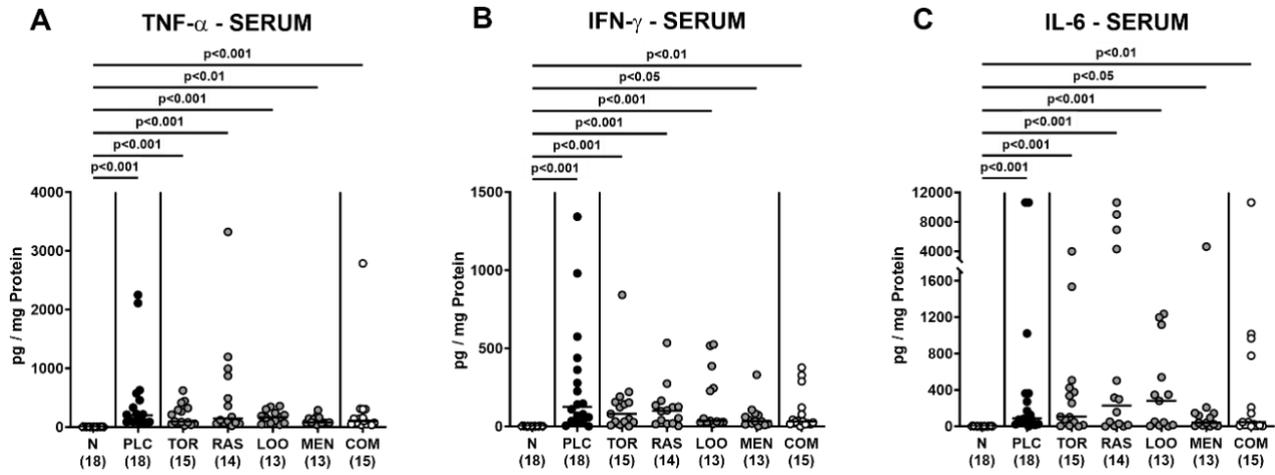
Supplementary Figure S3. Representative photomicrographs illustrating microscopic inflammatory changes following oral treatment of infected gut microbiota-depleted $IL-10^{-/-}$ mice with distinct natural compounds alone or in combination. Mice were orally infected with *C. jejuni* 81-176 strain on days 0 and 1. From day 2 until day 6, mice were treated with either tormentil (TOR), raspberry leaves (RAS), loosestrife (LOO), and menthol (MEN) alone or with a combination of all four compounds (COM) via the drinking water. Placebo control mice received vehicle only (PLC), whereas naive mice (N) served as uninfected and untreated controls. Photomicrographs representative of four independent experiments illustrate (A) colonic histopathological changes in hematoxylin and eosin (H&E) stained colonic paraffin sections (100x magnification; scale bar 100 μ m) and (B) apoptotic colonic epithelial cells in large intestinal paraffin sections positive for cleaved caspase-3 (100x magnification, scale bar 100 μ m) on day 6 post-infection.



Supplementary Figure S4: Pro-inflammatory cytokine secretion in the liver following oral treatment of infected gut microbiota depleted IL-10^{-/-} mice with distinct natural compounds alone or in combination. Mice were orally infected with *C. jejuni* 81-176 strain on days 0 and 1. From day 2 until day 6, mice were treated with either tormentil (TOR), raspberry leaves (RAS), loosestrife (LOO), and menthol (MEN) alone or with a combination of all four compounds (COM) via the drinking water. Placebo control mice received vehicle only (PLC), whereas naive mice (N) served as uninfected and untreated controls. On day 6 post-infection, (A) TNF- α , (B) IFN- γ , and (C) IL-6 concentrations were measured in liver explants. Medians (black bars), significance levels (p values) determined by the Kruskal-Wallis test with Dunn's multiple comparison test and numbers of mice included from three independent experiments (in parentheses) are indicated.



Supplementary Figure S5: Pro-inflammatory cytokine secretion in the kidneys following oral treatment of infected gut microbiota depleted IL-10^{-/-} mice with distinct natural compounds alone or in combination. Mice were orally infected with *C. jejuni* 81-176 strain on days 0 and 1. From day 2 until day 6, mice were treated with either tormentil (TOR), raspberry leaves (RAS), loosestrife (LOO), and menthol (MEN) alone or with a combination of all four compounds (COM) via the drinking water. Placebo control mice received vehicle only (PLC), whereas naive mice (N) served as uninfected and untreated controls. On day 6 post-infection, (A) TNF- α , (B) IFN- γ , and (C) IL-6 concentrations were measured in kidney explants. Medians (black bars), significance levels (p values) determined by the Kruskal-Wallis test with Dunn's multiple comparison test and numbers of mice included from three independent experiments (in parentheses) are indicated.



Supplementary Figure S6: Systemic pro-inflammatory cytokine secretion following oral treatment of infected gut microbiota depleted IL-10^{-/-} mice with distinct natural compounds alone or in combination. Mice were orally infected with *C. jejuni* 81-176 strain on days 0 and 1. From day 2 until day 6, mice were treated with either tormentil (TOR), raspberry leaves (RAS), loosestrife (LOO), and menthol (MEN) alone or with a combination of all four compounds (COM) via the drinking water. Placebo control mice received vehicle only (PLC), whereas naive mice (N) served as uninfected and untreated controls. On day 6 post-infection, (A) TNF- α , (B) IFN- γ , and (C) IL-6 concentrations were measured in serum samples. Medians (black bars), significance levels (p values) determined by the Kruskal-Wallis test with Dunn's multiple comparison test, and numbers of mice included from three independent experiments (in parentheses) are indicated.