

# Supplementary Information

## **Effect of dietary $\omega$ -3 fatty acids, ascorbic acid, and polyphenolic antioxidant flavonoid supplements on gene expression, organ failure and mortality in endotoxemic-induced septic rats.**

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### **SUPPLEMENTARY MATERIAL AND METHODS**

#### **Protein expression determination of RMEC by flow cytometry**

Flow cytometry analysis was performed to determine protein expression changes of VE-Cad,  $\alpha$ -SMA, Col III, TNF- $\alpha$ , and NF- $\kappa$ B using corresponding monoclonal antibodies (all from R&D Systems, Inc), coupled to suitable secondary antibodies conjugated to fluorophores (all from ThermoFisher). The labeled cells were then analyzed immediately by flow cytometry (BD FACS Fortessa, BD Biosciences, San José, CA). Color compensation matrices were calculated for each staining combination within each experiment using single-stained antibody. In all analyses, doublets and clusters were eliminated. A minimum of 10,000 events were analyzed.

#### **Statistical analyses**

The relationships between variables were assessed by means of correlation analysis using Spearman's correlation coefficients and linear regression. The data were analyzed with GraphPad Prism version 9.4 (GraphPad Software, LLC). Samples used in the study were defined to identify the mean magnitude effect of  $\geq 2$ -fold change with standard deviations of 10%. Accordingly, a sample size of 12 rats per groups, would provide 90% statistical power using a two-sided 0.05 significance level.

### **SUPPLEMENTARY TABLE LEGENDS**

**Supplementary Table S1. Correlation analyses between mRNA expression of EndMT genes and increased permeability in the mesentery, in endotoxemic condition.**  $r^2$ : correlation coefficient and  $p$ : p-value.

**Supplementary Table S2. Correlation analyses between mRNA expression of EndMT genes and increased permeability in the liver, in endotoxemic condition.**  $r^2$ : correlation coefficient and  $p$ : p-value.

**Supplementary Table S3. Correlation analyses between mRNA expression of EndMT genes and increased permeability in the kidney, in endotoxemic condition.**  $r^2$ : correlation coefficient and  $p$ : p-value.

**Supplementary Table S4. Summary of actions of dietary  $\omega$ -3 fatty acids, ascorbic acid, and polyphenolic antioxidant flavonoid supplements on gene expression, organ failure and mortality in endotoxemic-induced septic rats.**

#### **SUPPLEMENTARY FIGURE LEGENDS**

**Supplementary Figure S1. Impact on EndMT protein expression through dietary supplementation based on  $\omega$ -3 FA, ascorbic acid or polyphenolic antioxidant flavonoids in endotoxemic rats.** (A-D) The mRNA expression of EndMT markers (endothelial marker VE-Cadherin (red bars) and fibrotic and ECM markers  $\alpha$ -SMA and Coll III (green bars)), EndMT inducer TNF- $\alpha$  (green bars) and EndMT signaling transcription factor NF- $\kappa$ B (blue bars) were detected in rats subjected to endotoxemia and supplemented with  $\omega$ -3 fatty acid ( $\omega$ -3 FA, A and B), ascorbic acid (AsA, C and D) or polyphenolic antioxidant flavonoids (Flav, E and F) through a therapeutic (A, C and E) and a prophylactic (B, D and F) protocol. (G-L) Survival percentage was determined 7 days after endotoxemia induction in rats subjected to endotoxemia and supplemented with  $\omega$ -3 fatty acid ( $\omega$ -3 FA, G and H), ascorbic acid (AsA, I and J) or polyphenolic antioxidant flavonoids (Flav, K and L) through a therapeutic (G, I and K) and a prophylactic (H, J and L) protocol. Statistical differences were assessed by a one-way analysis of variance (ANOVA) (Kruskal–Wallis) followed by Dunn's *post hoc* test. \* $p < 0.05$ , \*\* $p < 0.01$ , \*\*\* $p < 0.001$  compared with the saline-treated condition. Determination of protein expression was normalized relative to  $\beta$ -tubulin expression and are expressed relative to sham-supplemented condition. Values are expressed as the mean  $\pm$  SD. ( $N = 12$ ).

# Supplementary Table S1

## Mesentery permeability in endotoxemic rats (Evans Blue dye (ng/mg))

mRNA expression  
(Log2 (fold change))

		prophylactic ↓ therapeutic	sham ↓ sham	sham ↓ ω-3FA	ω-3FA ↓ ω-3FA	sham ↓ AsA	AsA ↓ AsA	sham ↓ Flav	Flav ↓ Flav
		r <sup>2</sup> p	r <sup>2</sup> p	r <sup>2</sup> p	r <sup>2</sup> p	r <sup>2</sup> p	r <sup>2</sup> p	r <sup>2</sup> p	r <sup>2</sup> p
EndMT markers	Endothelial proteins	VE-Cad	<b>0.843</b> <b>0.002</b>	<b>0.820</b> <b>0.005</b>	<b>0.812</b> <b>0.006</b>	<b>0.801</b> <b>0.012</b>	<b>0.823</b> <b>0.008</b>	<b>0.804</b> <b>0.002</b>	<b>0.823</b> <b>0.004</b>
		PECAM	0.623 0.034	0.763 0.010	0.723 0.009	<b>0.833</b> <b>0.011</b>	0.775 0.009	0.635 0.012	0.735 0.009
		vWF	0.645 0.023	0.623 0.012	0.734 0.011	0.764 0.026	<b>0.801</b> <b>0.007</b>	0.624 0.027	<b>0.812</b> <b>0.008</b>
		Col IV	0.753 0.026	<b>0.827</b> <b>0.002</b>	0.745 0.030	0.524 0.045	0.597 0.042	0.634 0.021	<b>0.824</b> <b>0.011</b>
	Fibrotic and ECM proteins	α-SMA	<b>0.853</b> <b>0.005</b>	<b>0.864</b> <b>0.006</b>	<b>0.867</b> <b>0.006</b>	<b>0.832</b> <b>0.005</b>	<b>0.826</b> <b>0.007</b>	<b>0.821</b> <b>0.006</b>	<b>0.888</b> <b>0.004</b>
		SM22α	0.684 0.023	0.734 0.023	0.742 0.022	0.753 0.014	0.763 0.003	0.724 0.021	0.423 0.108
		FSP-1	<b>0.824</b> <b>0.003</b>	0.724 0.064	<b>0.832</b> <b>0.023</b>	0.628 0.023	<b>0.812</b> <b>0.012</b>	0.535 0.086	0.684 0.044
		Col I	0.712 0.032	0.702 0.021	<b>0.821</b> <b>0.007</b>	0.636 0.033	<b>0.831</b> <b>0.025</b>	0.603 0.034	0.762 0.048
		Col III	<b>0.821</b> <b>0.003</b>	<b>0.808</b> <b>0.004</b>	<b>0.814</b> <b>0.006</b>	<b>0.834</b> <b>0.007</b>	<b>0.845</b> <b>0.008</b>	<b>0.863</b> <b>0.008</b>	<b>0.835</b> <b>0.004</b>
		FN	0.734 0.036	0.745 0.021	0.636 0.022	0.574 0.052	0.652 0.015	0.425 0.104	7.352 0.018
	EndMT inducers	IL-1β	0.634 0.021	0.693 0.032	0.685 0.034	0.625 0.023	0.734 0.015	0.636 0.034	0.424 0.121
		IL-6	0.735 0.023	0.753 0.022	0.734 0.045	0.536 0.055	0.634 0.010	0.735 0.021	0.635 0.037
		TNF-α	<b>0.825</b> <b>0.034</b>	<b>0.814</b> <b>0.006</b>	<b>0.842</b> <b>0.010</b>	<b>0.824</b> <b>0.009</b>	<b>0.864</b> <b>0.005</b>	<b>0.853</b> <b>0.010</b>	<b>0.912</b> <b>0.002</b>
		TGF-β1	0.636 0.045	0.746 0.024	0.536 0.052	0.536 0.034	0.536 0.580	0.523 0.041	0.724 0.027
		TGF-β2	0.536 0.051	0.723 0.015	0.743 0.023	0.423 0.127	0.585 0.056	0.423 0.098	<b>0.845</b> <b>0.043</b>
EndMT signaling	Receptors	IL1R	<b>0.842</b> <b>0.004</b>	0.734 0.011	<b>0.826</b> <b>0.003</b>	0.734 0.021	<b>0.842</b> <b>0.003</b>	0.653 0.037	0.724 0.023
		IL6R	0.765 0.022	0.786 0.032	0.783 0.032	0.535 0.057	0.712 0.018	0.646 0.043	0.635 0.043
		TNFR	0.698 0.023	0.647 0.042	0.742 0.004	0.634 0.010	0.685 0.021	0.647 0.034	<b>0.824</b> <b>0.005</b>
		TβRI	0.774 0.021	0.542 0.053	0.636 0.032	0.425 0.245	0.535 0.075	0.636 0.045	0.746 0.026
		TβRII	0.686 0.043	0.577 0.046	0.684 0.031	0.486 0.174	0.596 0.067	0.643 0.041	0.735 0.021
	Transcription factors	NF-κB	<b>0.824</b> <b>0.007</b>	<b>0.802</b> <b>0.007</b>	<b>0.875</b> <b>0.002</b>	<b>0.823</b> <b>0.005</b>	<b>0.821</b> <b>0.003</b>	<b>0.834</b> <b>0.008</b>	<b>0.874</b> <b>0.009</b>
		Smad4	<b>0.802</b> <b>0.010</b>	0.746 0.009	<b>0.807</b> <b>0.008</b>	0.654 0.047	0.533 0.026	0.745 0.012	0.635 0.026
		Slug	<b>0.806</b> <b>0.005</b>	0.775 0.021	0.735 0.008	0.685 0.026	0.643 0.021	0.723 0.008	<b>0.801</b> <b>0.005</b>
		Twist	0.753 0.008	0.720 0.014	0.723 0.005	0.698 0.021	0.585 0.044	0.742 0.011	0.702 0.008
		Snail	0.798 0.004	0.635 0.047	0.646 0.035	0.497 0.102	0.573 0.048	0.634 0.019	0.612 0.034
		Zeb-1	<b>0.832</b> <b>0.007</b>	0.684 0.044	0.635 0.034	0.553 0.086	0.578 0.047	0.647 0.021	0.621 0.041
	ROS enzymes	NOX-1	0.435 0.224	0.325 0.284	0.224 0.533	0.475 0.285	0.474 0.446	0.412 0.523	0.353 0.224
		NOX-2	0.723 0.034	0.712 0.011	0.646 0.023	0.634 0.036	0.774 0.032	0.653 0.023	0.474 0.103
		NOX-4	0.423 0.335	0.446 0.274	0.436 0.324	0.424 0.425	0.335 0.536	0.523 0.324	0.536 0.475

# Supplementary Table S2

## Liver permeability in endotoxemic rats (Evans Blue dye (ng/mg))

### mRNA expression (Log2 (fold change))

			prophylactic ↓ therapeutic	sham ↓ sham		sham ↓ ω-3FA		ω-3FA ↓ ω-3FA		sham ↓ AsA		AsA ↓ AsA		sham ↓ Flav		Flav ↓ Flav	
			r <sup>2</sup>	p	r <sup>2</sup>	p	r <sup>2</sup>	p	r <sup>2</sup>	p	r <sup>2</sup>	p	r <sup>2</sup>	p	r <sup>2</sup>	p	
EndMT markers	Endothelial proteins	VE-Cad	<b>0.853</b>	<b>0.007</b>	<b>0.804</b>	<b>0.004</b>	<b>0.864</b>	<b>0.003</b>	<b>0.853</b>	<b>0.004</b>	<b>0.864</b>	<b>0.004</b>	<b>0.843</b>	<b>0.003</b>	<b>0.812</b>	<b>0.008</b>	
		PECAM	0.745	0.017	0.722	0.041	<b>0.846</b>	<b>0.004</b>	<b>0.821</b>	<b>0.002</b>	<b>0.853</b>	<b>0.004</b>	0.664	0.014	<b>0.801</b>	<b>0.008</b>	
		vWF	0.698	0.032	0.698	0.049	0.744	0.022	<b>0.802</b>	<b>0.007</b>	0.746	0.004	0.675	0.018	0.753	0.012	
		Col IV	0.724	0.021	0.753	0.036	0.646	0.048	0.643	0.046	0.636	0.041	0.646	0.031	0.732	0.023	
	Fibrotic and ECM proteins	α-SMA	<b>0.842</b>	<b>0.004</b>	<b>0.864</b>	<b>0.007</b>	<b>0.864</b>	<b>0.006</b>	<b>0.853</b>	<b>0.005</b>	<b>0.825</b>	<b>0.005</b>	<b>0.806</b>	<b>0.002</b>	<b>0.824</b>	<b>0.005</b>	
		SM22α	<b>0.842</b>	<b>0.006</b>	0.721	0.032	<b>0.857</b>	<b>0.003</b>	<b>0.845</b>	<b>0.005</b>	0.637	0.024	0.773	0.043	0.735	0.108	
		FSP-1	<b>0.817</b>	<b>0.005</b>	0.774	0.048	<b>0.835</b>	<b>0.006</b>	0.646	0.510	0.753	0.023	0.685	0.045	0.634	0.034	
		Col I	0.634	0.045	<b>0.808</b>	<b>0.004</b>	<b>0.854</b>	<b>0.003</b>	0.735	0.511	<b>0.864</b>	<b>0.034</b>	0.745	0.019	0.628	0.046	
		Col III	<b>0.864</b>	<b>0.008</b>	<b>0.853</b>	<b>0.005</b>	<b>0.847</b>	<b>0.007</b>	<b>0.863</b>	<b>0.006</b>	<b>0.852</b>	<b>0.009</b>	<b>0.808</b>	<b>0.004</b>	<b>0.823</b>	<b>0.002</b>	
		FN	0.674	0.043	0.747	0.17	<b>0.864</b>	<b>0.003</b>	0.657	0.271	0.736	0.028	0.545	0.164	<b>0.865</b>	<b>0.003</b>	
	EndMT inducers	IL-1β	0.654	0.031	0.743	0.025	<b>0.831</b>	<b>0.025</b>	0.746	0.31	0.732	0.043	0.745	0.017	0.545	0.041	
		IL-6	0.636	0.041	0.635	0.032	0.675	0.034	0.675	0.042	0.753	0.021	0.712	0.014	0.546	0.045	
		TNF-α	<b>0.845</b>	<b>0.006</b>	<b>0.821</b>	<b>0.004</b>	<b>0.802</b>	<b>0.007</b>	<b>0.827</b>	<b>0.004</b>	<b>0.857</b>	<b>0.003</b>	<b>0.835</b>	<b>0.003</b>	<b>0.845</b>	<b>0.003</b>	
		TGF-β1	0.674	0.036	0.690	0.032	0.547	0.185	0.623	0.042	0.636	0.032	0.635	0.047	0.646	0.076	
		TGF-β2	0.612	0.042	0.775	0.009	0.528	0.123	0.546	0.164	0.585	0.041	0.546	0.232	0.536	0.051	
EndMT signaling	Receptors	IL1R	<b>0.832</b>	<b>0.006</b>	0.743	0.023	0.747	0.024	0.652	0.164	<b>0.825</b>	<b>0.023</b>	0.753	0.024	0.735	0.034	
		IL6R	0.698	0.016	0.734	0.018	<b>0.863</b>	<b>0.008</b>	0.754	0.076	0.753	0.015	0.710	0.019	0.743	0.043	
		TNFR	0.735	0.025	0.763	0.037	<b>0.844</b>	<b>0.002</b>	0.523	0.274	0.735	0.024	0.764	0.024	0.724	0.024	
		TβRI	0.586	0.052	0.634	0.034	0.735	0.085	0.525	0.253	0.628	0.023	0.724	0.023	<b>0.846</b>	<b>0.003</b>	
		TβRII	0.596	0.580	0.624	0.032	0.636	0.143	0.567	0.324	0.535	0.045	0.647	0.042	<b>0.854</b>	<b>0.004</b>	
	Transcription factors	NF-κB	<b>0.842</b>	<b>0.004</b>	<b>0.832</b>	<b>0.005</b>	<b>0.864</b>	<b>0.001</b>	<b>0.853</b>	<b>0.003</b>	<b>0.815</b>	<b>0.004</b>	<b>0.834</b>	<b>0.003</b>	<b>0.843</b>	<b>0.005</b>	
		Smad4	<b>0.864</b>	<b>0.003</b>	0.724	0.013	<b>0.807</b>	<b>0.003</b>	0.763	0.042	<b>0.811</b>	<b>0.023</b>	0.723	0.032	0.685	0.034	
		Slug	0.753	0.078	0.746	0.035	<b>0.802</b>	<b>0.005</b>	<b>0.835</b>	<b>0.002</b>	0.843	0.004	0.754	0.042	<b>0.832</b>	<b>0.006</b>	
		Twist	<b>0.824</b>	<b>0.006</b>	<b>0.823</b>	<b>0.003</b>	0.642	0.632	0.735	0.033	0.734	0.032	0.742	0.034	0.708	0.003	
		Snail	<b>0.835</b>	<b>0.008</b>	0.735	0.414	0.753	0.032	0.585	0.153	0.698	0.038	0.635	0.051	0.536	0.046	
		Zeb-1	<b>0.835</b>	<b>0.009</b>	0.692	0.053	0.732	0.043	0.532	0.065	0.654	0.042	0.546	0.075	0.586	0.042	
	ROS enzymes	NOX-1	0.425	0.367	0.374	0.375	0.353	0.364	0.374	0.296	0.536	0.275	0.535	0.343	0.435	0.453	
		NOX-2	0.794	0.021	0.734	0.021	0.725	0.012	0.764	0.027	<b>0.853</b>	<b>0.007</b>	0.744	0.034	0.743	0.027	
		NOX-4	0.512	0.275	0.375	0.353	0.374	0.243	0.374	0.346	0.475	0.335	0.524	0.243	0.635	0.335	

# Supplementary Table S3

## kidney permeability in endotoxemic rats (Evans Blue dye (ng/mg))

### mRNA expression (Log2 (fold change))

			prophylactic ↓ therapeutic		sham ↓ sham		sham ↓ ω-3FA		ω-3FA ↓ ω-3FA		sham ↓ AsA		AsA ↓ AsA		sham ↓ Flav		Flav ↓ Flav						
			r <sup>2</sup>		p		r <sup>2</sup>		p		r <sup>2</sup>		p		r <sup>2</sup>		p		r <sup>2</sup>		p		
EndMT markers	Endothelial proteins	VE-Cad	<b>0.813</b>	<b>0.009</b>		<b>0.853</b>	<b>0.007</b>		<b>0.842</b>	<b>0.002</b>		<b>0.813</b>	<b>0.006</b>		<b>0.823</b>	<b>0.003</b>		<b>0.832</b>	<b>0.004</b>		<b>0.823</b>	<b>0.006</b>	
		PECAM	0.735	0.14		0.754	0.025		<b>0.814</b>	<b>0.003</b>		<b>0.804</b>	<b>0.008</b>		<b>0.831</b>	<b>0.005</b>		0.745	0.011		0.703	0.038	
		vWF	0.743	0.16		0.536	0.043		<b>0.834</b>	<b>0.031</b>		0.735	0.023		0.723	0.032		0.634	0.031		<b>0.843</b>	<b>0.006</b>	
		Col IV	0.757	0.15		0.647	0.023		0.753	0.023		0.712	0.056		0.721	0.024		0.628	0.023		0.754	0.034	
	Fibrotic and ECM proteins	α-SMA	<b>0.843</b>	<b>0.005</b>		<b>0.821</b>	<b>0.003</b>		<b>0.853</b>	<b>0.006</b>		<b>0.813</b>	<b>0.003</b>		<b>0.821</b>	<b>0.003</b>		<b>0.812</b>	<b>0.004</b>		<b>0.864</b>	<b>0.001</b>	
		SM22α	<b>0.814</b>	<b>0.007</b>		<b>0.842</b>	<b>0.007</b>		<b>0.876</b>	<b>0.003</b>		<b>0.821</b>	<b>0.002</b>		0.734	0.034		0.743	0.043		0.742	0.047	
		FSP-1	<b>0.822</b>	<b>0.003</b>		0.742	0.017		<b>0.824</b>	<b>0.006</b>		0.623	0.232		<b>0.832</b>	<b>0.002</b>		0.712	0.047		0.697	0.041	
		Col I	0.753	0.034		0.764	0.023		0.753	0.006		0.653	0.423		0.702	0.045		0.624	0.041		<b>0.843</b>	<b>0.006</b>	
		Col III	<b>0.842</b>	<b>0.003</b>		<b>0.824</b>	<b>0.002</b>		<b>0.846</b>	<b>0.007</b>		<b>0.823</b>	<b>0.005</b>		<b>0.812</b>	<b>0.007</b>		<b>0.834</b>	<b>0.002</b>		<b>0.803</b>	<b>0.003</b>	
		FN	0.721	0.034		<b>0.815</b>	<b>0.004</b>		<b>0.823</b>	<b>0.003</b>		0.694	0.150		0.701	0.032		0.635	0.059		0.745	0.043	
	EndMT inducers	IL-1β	0.665	0.031		0.713	0.012		<b>0.853</b>	<b>0.003</b>		0.702	0.037		0.712	0.032		<b>0.832</b>	<b>0.002</b>		0.624	0.021	
		IL-6	0.745	0.024		0.743	0.010		0.742	0.031		0.643	0.039		0.701	0.023		<b>0.875</b>	<b>0.001</b>		0.657	0.042	
		TNF-α	<b>0.864</b>	<b>0.008</b>		<b>0.813</b>	<b>0.006</b>		<b>0.843</b>	<b>0.004</b>		<b>0.823</b>	<b>0.002</b>		<b>0.822</b>	<b>0.004</b>		<b>0.823</b>	<b>0.004</b>		<b>0.812</b>	<b>0.006</b>	
		TGF-β1	0.756	0.024		0.535	0.143		0.634	0.243		0.732	0.021		0.612	0.047		0.745	0.032		0.536	0.054	
		TGF-β2	0.626	0.45		0.723	0.087		0.646	0.353		0.624	0.244		0.633	0.038		0.632	0.045		0.684	0.067	
	EndMT signaling	Receptors	IL1R	<b>0.846</b>	<b>0.005</b>		0.735	0.032		0.742	0.018		0.732	0.032		0.742	0.032		0.723	0.034		0.793	0.041
			IL6R	0.753	0.021		0.712	0.039		0.635	0.021		<b>0.842</b>	<b>0.003</b>		0.767	0.022		0.624	0.045		<b>0.821</b>	<b>0.006</b>
			TNFR	0.646	0.032		0.756	0.041		0.754	0.026		0.643	0.046		<b>0.834</b>	<b>0.005</b>		0.734	0.037		<b>0.902</b>	<b>0.002</b>
			TβRI	0.635	0.028		0.748	0.043		0.642	0.038		0.597	0.142		0.745	0.034		0.634	0.047		<b>0.843</b>	<b>0.004</b>
TβRII			0.685	0.034		0.623	0.053		0.746	0.033		0.643	0.243		0.646	0.040		0.697	0.049		0.723	0.023	
Transcription factors		NF-κB	<b>0.853</b>	<b>0.003</b>		<b>0.825</b>	<b>0.007</b>		<b>0.824</b>	<b>0.003</b>		<b>0.832</b>	<b>0.002</b>		<b>0.804</b>	<b>0.005</b>		<b>0.823</b>	<b>0.005</b>		<b>0.854</b>	<b>0.007</b>	
		Smad4	<b>0.854</b>	<b>0.002</b>		0.765	0.010		0.745	0.034		0.734	0.023		0.744	0.032		0.723	0.043		0.732	0.041	
		Slug	<b>0.824</b>	<b>0.003</b>		0.643	0.042		<b>0.844</b>	<b>0.004</b>		0.753	0.021		0.795	0.012		0.721	0.038		<b>0.832</b>	<b>0.005</b>	
		Twist	<b>0.864</b>	<b>0.002</b>		0.647	0.044		<b>0.864</b>	<b>0.002</b>		0.744	0.026		<b>0.832</b>	<b>0.004</b>		0.657	0.043		0.634	0.041	
		Snail	0.753	0.015		0.753	0.021		0.647	0.040		0.634	0.046		0.753	0.022		0.686	0.048		0.684	0.042	
		Zeb-1	<b>0.832</b>	<b>0.006</b>		0.785	0.015		0.624	0.048		0.647	0.048		0.634	0.054		0.676	0.049		0.623	0.047	
ROS enzymes	NOX-1	0.524	0.285		0.435	0.453		0.536	0.364		0.435	0.321		0.435	0.285		0.634	0.104		0.474	0.224		
	NOX-2	<b>0.853</b>	<b>0.007</b>		0.745	0.032		<b>0.834</b>	<b>0.002</b>		0.735	0.023		<b>0.845</b>	<b>0.006</b>		0.721	0.038		<b>0.834</b>	<b>0.004</b>		
	NOX-4	0.684	0.087		0.536	0.078		0.446	0.007		0.495	0.335		0.423	0.242		0.635	0.098		0.423	0.243		

## Supplementary Table S4

**Supplementary Table S4.** Summary of actions of dietary  $\omega$ -3 fatty acids, ascorbic acid, and polyphenolic antioxidant flavonoid supplements on gene expression, organ failure and mortality in endotoxemic-induced septic rats.

		Supplementation:	Sham	$\omega$ -3 Fatty acid		Ascorbid Acid		Flavonoid	
		Protocol:		Therapeutic	Prophylactic	Therapeutic	Prophylactic	Therapeutic	Prophylactic
Gene expression	EndMT markers	VE-Cad	**	*	NS	**	*	*	NS
		PECAM	**	NS	NS	**	*	*	NS
		vWF	**	NS	NS	**	*	*	NS
		Col IV	***	*	*	**	*	*	NS
		$\alpha$ -SMA	***	*	NS	***	*	**	NS
		SM22 $\alpha$	***	*	*	***	*	*	*
		FSP-1	***	NS	NS	*	*	*	NS
		Col I	***	NS	NS	*	*	**	NS
		Col III	***	NS	NS	***	**	***	NS
		FN	***	NS	NS	***	**	***	NS
	EndMT inducers	IL-1 $\beta$	***	NS	NS	***	**	***	NS
		IL-6	**	NS	NS	*	*	*	NS
		TNF- $\alpha$	***	*	*	**	*	*	*
		TGF- $\beta$ 1	***	NS	NS	**	*	**	NS
		TGF- $\beta$ 2	**	NS	NS	*	*	*	NS
	EndMT signaling	IL1R	***	*	NS	**	***	***	NS
		IL6R	***	*	NS	**	***	***	NS
		TNFR	***	**	*	***	***	***	*
		T $\beta$ RI	*	*	NS	NS	NS	NS	NS
		T $\beta$ RII	NS	NS	NS	NS	NS	NS	NS
		NF- $\kappa$ B	***	**	NS	***	***	**	NS
		Smad4	***	**	NS	***	***	**	NS
		Slug	***	**	NS	***	***	**	NS
		Twist	***	*	NS	**	***	**	NS
		Snail	***	*	NS	***	***	**	NS
		Zeb-1	***	**	NS	**	*	**	NS
		NOX-1	NS	NS	NS	NS	NS	NS	NS
		NOX-2	***	**	*	**	*	*	*
		NOX-4	NS	NS	NS	NS	NS	NS	NS
Vascular permeability	Mesentery	***	**	*	***	**	**	**	**
	Liver	***	**	*	***	**	***	**	**
	Kidney	***	**	NS	***	***	***	**	**
Non-survivor Vascular permeability	Mesentery	*	*	*	NS	NS	NS	*	*
	Liver	*	*	*	NS	NS	NS	*	*
	Kidney	*	*	*	NS	NS	NS	*	*
Systolic pressure		***	***	*	***	***	***	***	**
Heart rate		***	**	NS	***	***	***	***	**
MODS	ALT	***	**	NS	***	***	***	***	**
	AST	***	**	*	***	***	***	***	**
	TBIL	***	**	*	***	***	***	***	***
	GGT	***	**	NS	***	***	**	*	*
	Lac	***	**	*	***	***	***	***	***
	CRE	***	**	*	**	**	**	**	*
	BUN	***	**	*	**	**	**	**	**
	BUN/CRE	***	***	NS	***	***	***	***	***
	eGFR	**	**	NS	**	**	**	**	**
	Gly	**	*	NS	**	**	**	**	**
Mortality at 7 days		75 %	50 %	17 %	75 %	67 %	67 %	50 %	
Risk of death		‡‡‡	NS	NS	‡‡‡	‡‡	‡‡	NS	

\*: p-value < 0.05; \*\*: p-value < 0.01; \*\*\*: p-value < 0.001; ‡: p-value < 0.05; ‡‡: p-value < 0.01; NS: non-significant change. All compared with saline-treated rats.

Supplementary Figure S1

