A review on the effects of flavan-3-ols, their metabolites, and their dietary sources on gut barrier integrity.

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Supplementary Material

Table 1. Overview of the *in vitro*, *ex vivo,* and animal studies reporting the effects of products containing flavan-3-ols and derivatives compounds on markers of the gut barrier integrity. Summary of main results have been organised by food source (cocoa, pome fruit, berries, tea, grape, and other minor classes) or individual compound analysed.

Ref.	Model cell/animal	Stressor (S)	PP/S exposure	(Poly)phenol source (PP)	Tested PP conc./quantity	Effect(s)
Cocoa						
1	Caco-2		0.5h (PP)	Cocoa extract mainly hexamers	10 µM	Permeability (Para) ↔
			0-2h (PP)	Cocoa extract mainly hexamers	20 µM	TEER TD ↑
		DCA (0.2 mM)	0.5h (PP) → 6h (PP+S)	Cocoa extract mainly hexamers	10 µM	ProtX (ZO-1) ↓^{X}. Loc (ZO-1) change^{X}
		AMVN (10 mM)	0.5h (PP) → 1h (S)	Cocoa extract mainly hexamers	10 µM	Permeability (Para) ↑^{X}
2	Caco-2	DSS (2%)	2h (PP) → 48h (PP+S)	Cocoa extract, cocoa extract with mainly monomers, cocoa extract with mainly oligomers	100 µg/mL	Permeability ↑^{X}
				Cocoa extract with mainly polymers	10, 25, and 100 µg/mL	Permeability ↑^{X}
3	C57BL/6J mice (*n* = 21-24, 4wk, 100%)	HFD	126d (S+PP)	Unsweetened cocoa powder	80 mg/g diet	Permeability (Endotoxin) ↑^{X}, (GLP-2) ↓^{X}
4	C57BL/6 obese mice (*n* = 12, 4wk, ≥ 23.1g, 50%)	HFD	56d (S) → 56d (S+PP)	Seven different compositions of cocoa powder	80 mg/g diet/day (35.7 – 65.9 mg GAE/g powder)	Permeability (FITC-Dx, LPS, LBP) ↑^{X}
5	Zucker diabetic fatty rats (*n* = 8,	Diabetes and BW	70d (PP)	Forastero cocoa powder	100 g/kg diet/day	ProtX (ZO-1) ↓^{X}. Mucus glycoproteins ↑. Crypt depth ↑

	9wk, 100%)					
6	Sprague-Dawley rats (n = 14, 8wk, 0%)	Loperamide (5 mg/kg/day)	14d (PP+S)	Chocolate	50 mg/day	Permeability (FITC-Dx) ↔$^{\varnothing}$ MPO ↔$^{\varnothing}$ GenX (ZO-1) ↓^{X}, (ZO-1 & CL-1, ileum) ↔$^{\varnothing}$, (Occ)↓$^{\varnothing}$, (CL-1) ↑$^{\varnothing}$ Mucus thickness ↓$^{\varnothing}$ GC n. ↔$^{\varnothing}$
				Probiotic chocolate with *Streptococcus thermophilus* MG510 & *Lactobacillus plantarum* LRCC51936	50 mg/day	Permeability (FITC-Dx) ↔$^{\varnothing}$. MPO ↔$^{\varnothing}$. GenX (ZO-1, OCC) ↓^{X}, (ZO-1 & CL-1, ileum) ↔$^{\varnothing}$, (CL-1) ↑^{X}. Mucus thickness ↓^{X}. GC n. ↔$^{\varnothing}$
7	Sprague–Dawley rats (n = 12, 8wk, 185-195g, 0%)	Loperamide (5 mg/kg/day)	21d (PP) →7d (PP+S)	Chocolate	50 mg/day	Permeability (FITC-Dx) ↑$^{\varnothing}$. GenX (ZO-1 & OCC & CL-1 & Muc2) ↔. GC n. ↔$^{\varnothing}$
				Probiotic chocolate with *Streptococcus thermophilus* MG510 & *Lactobacillus plantarum* LRCC51936	50 mg/day	Permeability (FITC-Dx) ↑$^{\varnothing}$. GenX (ZO-1 & OCC & CL-1 & Muc2) ↑. GC n. ↔$^{\varnothing}$
				Probiotic chocolate with *Bifidobacterium animalis* subsp. *lactis*	50 mg/day	Permeability (FITC-Dx) ↑^{X}. GenX (ZO-1 & OCC) ↔, (CL-1 & Muc2) ↑. GC n. ↔$^{\varnothing}$
Pome fruits						
8	Caco-2	LPS (50 µg/mL)	24h (PP+S)	Granny Smith apple extract with (+)-catechin and (–)-epicatechin as main compounds, Granny Smith apple extract with chlorogenic acid as main compound, Granny Smith apple extract with PC Trimer	12.5 µg/mL	ProtX (ZO-1 & OCC) ↓$^{\varnothing}$
					25 and 50 µg/mL	ProtX (ZO-1) ↓^{X}, (OCC) ↓$^{\varnothing}$
					100 µg/mL	ProtX (ZO-1 & OCC) ↓^{X}

				C1 as main compound		
				Granny Smith apple extract with PC B2 as main compound	12.5 µg/mL	ProtX (ZO-1 & OCC) ↓$^{\emptyset}$
					25 µg/mL	ProtX (ZO-1) ↓^{X}, (OCC) ↓$^{\emptyset}$
			6h-24h (PP+S)	Granny Smith apple extract with PC B2 as main compound	50 µg/mL	ProtX & GenX (ZO-1) ↓^{X}, (OCC) ↓$^{\emptyset}$
					100 and 150 µg/mL	ProtX & GenX (ZO-1 & OCC) ↓^{X}
9	IPEC-J2		24h (PP)	Apple polyphenols	10, 20, and 40 µg/mL	ProtX (ZO-1 & OCC & CL-1) ↑
		ML-385 (5 µM)	24h (PP+S)	Apple polyphenols	40 µg/mL	ProtX (ZO-1 & OCC & CL-1) ↓^{X}
	Duroc × Landrace × Yorkshire pigs (*n* = 12, 71.25 kg)		49d (PP x 3 times/day)	Apple polyphenols	400 mg/kg	ProtX (ZO-1 & Occ & CL-1, jejunum) ↑. Villi tight (ileum & jejunum) ↑
					800 mg/kg	ProtX (ZO-1 & OCC, jejunum) ↑, (CL-1, jejunum) ↔. Villi tightness (ileum & jejunum) ↑
10	Sprague Dawley rats (*n* = 6, 5wk, 100%)	HFD	14d (S) → 56d (S+PP)	*Pyracantha fortuneana* (Maxim.) H. L. Li extract	0.4% diet	Permeability (L/M) ↑^{X}. ProtX (ZO-1 & OCC, jejunum) ↓^{X}. GenX (ZO-1, jejunum) ↓$^{\emptyset}$, (OCC, jejunum) ↔$^{\emptyset}$. Widened villi (intestinal) ↑^{X}
					1% diet	Permeability (L/M) ↑^{X}. ProtX & GenX (ZO-1, jejunum) ↓^{X}, (OCC, jejunum) ↔$^{\emptyset}$. Widened villi (intestinal) ↑^{X}
11	Caco-2		24h and 48h (PP)	Extract from apple waste	0.1, 0.05, and 0.01%	TEER TD ↑
					0.02%	TEER ↔
12	F344 rats (*n* = 4-12, 100%)	HFD + DMH	1d (S, DMH) → 7d LFD → 105d (S, HDF+PP)	Lyophilised (poly)phenols rich Marie Me'nard apples	7.6% w/w diet	Mucin depleted foci ↑^{X}
Berries						
13	Caco-2	LPS (2 µg/ml)	48h (PP+S)	Aronia berry powder	62.5 µg/mL	TEER ↓^{X}. GenX (ZO-1) ↓$^{\emptyset}$, (OCC & CL-1) ↔, (CL-3 & CL-4 & JAM-1) ↑
					125 µg/mL	TEER ↓^{X}. GenX (ZO-1) ↓$^{\emptyset}$, (OCC & CL-1 &

						CL-3 & CL-4 & JAM-1) ↔
					250 µg/mL	TEER ↓[X]. GenX (ZO-1) ↓[X]. (OCC & CL-1 & CL-3 & CL-4 & JAM-1) ↔
14	Caco-2	TNF-α (50 ng/mL) + IFN-γ (50 ng/mL) + IL-1β (25 ng/mL) + LPS (1 mg/mL)	24h (PP+S)	Aronia berry powder	0.5 - 10mg/mL	TEER ↓[X]
			0-24h (PP+S)	Aronia berry powder	2.4 mg/mL	TEER TD ↓[X]
			24h (PP+S, TEER & Permeability). 12h (PP+S, TJs)	Aronia berry powder	5 mg/mL	TEER ↓[X]. Permeability ↑[X]. GenX (ZO-1) ↑, (OCC) ↔[ø] ProtX (ZO-1 & OCC) ↓[X], (CL-1) ↑[X], (CL-4) ↑[ø]. Loc (ZO-1 & OCC) change[X]
15	Wistar rats (*n* = 8, 200-220g, 100%)	HFD	56d (S+PP)	Blueberry powder	10% w/w diet	Permeability (LBP) ↓. GenX (Muc2, ileum) ↑. Villus height (ileum) ↓[X]. GC density ↓[X]
16	C57BL/6 mice (*n* = 12, 8wk, 100%)	HFHS	56d (S+PP)	Cloudberry (*Rubus chamaemorus* L.), Alpine bearberry (*Arctostaphylos alpina* L. Spreng.), Lingonberry (*Vaccinium vitisidaea* L.)	200 mg powdered extract/kg BW	Permeability (LPS) ↑[X]. GenX (ZO-1 & Occ, jejunum & colon) ↔[ø]
				Bog blueberry (*Vaccinium uliginosum* L.), Crowberry (*Empetrum nigrum* L.)	200 mg powdered extract/kg BW	Permeability (LPS) ↑[ø]. GenX (ZO-1 & OCC, jejunum & colon) ↔[ø]
17	C57BL/6J mice (*n* = 12, 6wk, 100%)	HFHS	56d (S+PP)	Wild blueberry PACs, Wild blueberry PP fraction, Wild blueberry PP oligomers	200 mg/kg (17 – 53 mg PP/day)	Mucus thickness ↓[X]. Crypt depth ↔[ø]. GC density ↔[ø]
				Wild blueberry PACs	37 mg/kg	Mucus thickness ↓[X]. Crypt depth ↔[ø]. GC density; ↑
18	C57BL/6 mice (*n* = 10, 6wk,	DSS (3% w/v in drinking	7d (S+PP)	Maqui berry powder	50 and 100 mg/kg BW/day	MPO ↑[X]

	100%)	H_2O)			(IGG)	
					200 mg/kg BW/day (IGG)	MPO ↑^X. ProtX (OCC) ↓^X
19	Balb/c mice (*n* = 6, 12-14wk, 19-35g, 100%)	TNBS (70µL, 100 mg/kg in EtOH 50%, RA)	1d (PP+S) → 4d (PP)	(Poly)phenolic Maqui extract	50mg/kg/day	Mucin content ↓^X. GC n. ↓^X
			7d (PP) → 1d (PP+S) → 4d (PP)	(Poly)phenolic Maqui extract	50mg/kg/day	Mucin content ↓^X. GC n. ↓^X
					1% w/v drinking H_2O	Permeability (D-mannitol & Endotoxin) ↑^X. GenX (ZO-1 & JAM-A, small intestine) ↓^X, (CL-2, small intestine) GenX ↑^X, (Muc4, small intestine) ↔^Ø
20	ICR mice (*n* = 14, 6-8wk, 100%)	EEN	2d recovery from intervention → 5d (S+PP)	Cranberry proanthocyanidins	8 mg/kg BW/day (IGG)	ProtX (Muc2) ↓^Ø. GC n. (intestine) ↓^Ø. Villi length ↔^Ø. Crypt depth ↓^Ø
					50 mg/kg BW/day (IGG)	ProtX (Muc2) ↓^Ø. GC n. (intestine) ↓^X. Villi length ↔^Ø. Crypt depth ↓^Ø
					100 mg/kg BW/day (IGG)	ProtX (Muc2) ↓^Ø. GC n. (intestine) ↓^X. Villi length ↔^Ø. Crypt depth ↓^Ø
21	C57BL/6J mice (*n* = 12, 8wk)	HFHS	56d (S+PP)	Cranberry extract	200 mg/kg/day	Permeability (LPS) ↑^X. GenX (Muc2) ↑, (Muc2, jejunum) ↔^Ø
22	$Apc^{min/+}$ C57BL/6J mice (*n* = 10, 4wk, 0%)	Apc gene mutation	84d (PP)	Freeze-dried whole cranberry	20% w/w diet	GenX (ZO-1 & CL-3) ↑. ProtX (Muc2) ↑
23	C57BL/6J mice (*n* = 8-12, 6wk, 100%)		42d (PP)	Dry red raspberry	5% w/w diet	ProtX (ZO-1) ↑, (OCC & CL-2 & CL-3) ↔. GenX (Muc2) ↔. Neutrophil infiltration score ↔
		DSS (2.5% w/v in H_2O)	28d (S) → 6d (S+PP) → 6d (S)	Dry red raspberry	5% w/w diet	ProtX (ZO-1) ↑, (Occ & CL-2) ↑^X, (CL-3) ↓^X. GenX (Muc) ↓^X. Neutrophil infiltration score ↑^X
24	C57BL/6J mice (*n* = 10, 6wk, 23.8 ± 1.0 g, 100%)	HFD	77d (S+PP)	Freeze-dried lingonberries batch 1	20% w/w diet	Permeability (LBP) ↓. GenX (OCC) ↑
				Freeze-dried lingonberries batch 2	20% w/w diet	Permeability (LBP) ↓. GenX (OCC) ↔
25	C57BL/6J mice (*n* = 8-12, 15-	LPS (300 µg/kg of	35d (PP) → 105d (PP+S)	Chinese Sweet Leaf Tea (*Rubus*	0.5% w/v drinking H_2O	Permeability (D-mannitol & endotoxin) ↑^X. GenX (ZO-1 & JAM-1, small intestine) ↓^X,

						(CL-2 & Muc4, small intestine) ↑
	16wk, 18-22g, 0%)	BW/day)		*suavissimus*)	1% w/v drinking H_2O	Permeability (D-mannitol &Endotoxin) ↑^{X}. GenX (ZO-1 & JAM-1, small intestine) ↓^{X}, (CL-2, small intestine) ↑^{X}, (Muc4, small intestine) ↔
Tea						
26	Caco-2		0-24h (PP)	Green tea extract	1 mg/mL	TEER ↑
		gliadin (1mg/mL)	0-24h (PP+S)	Green tea extract	1 mg/mL	TEER ↓^{X}
27	Caco-2		1-7d (PP), 7d (PP, TEER)	Green tea extract	10 ppm	TEER; TD ↑. GenX (ZO-1 & OCC & CL-2 & CL-3) ↑, (CL-15 & JAM-A) ↔
					100 ppm	TEER TD ↑. GenX (ZO-1 & Occ & CL-3 & CL-15 & JAM-A) ↔, (CL-2)↑
28	C57BL6/J mice (*n* = 10, 5wk, 100%)		84d (LFD) → 56d (LFD+PP)	Green tea extract	2% w/w diet	Permeability (Endotoxin) ↔. GenX (ZO-1 & OCC & CL-1, duodenum & jejunum& ileum) ↔
		HFD	84d (S) → 56d (S+PP)	Green tea extract	2% w/w diet	Permeability (Endotoxin) ↑^{X}. GenX (ZO-1 & OCC, duodenum & ileum) ↓^{X}, (CL-1, duodenum & jejunum & ileum) ↔^{Ø}, (ZO-1 & OCC, jejunum) ↔^{Ø}
29	WT mice (*n* = 20, 4wk)		56d (PP)	Green tea extract	2% w/w diet	Permeability (Endotoxin) ↓. GenX (ZO-1 & OCC, duodenum) ↔, (CL-1, duodenum & jejunum) ↑, (ZO-1 jejunum, CL-1 ileum) ↔, (OCC, jejunum) ↑, (ZO-1 & OCC, ileum) ↑
	TLR4m WT mice (*n* = 20, 4wk)	HFD & TLR4m function mutation	56d (S+PP)	Green tea extract	2% w/w diet	Permeability (Endotoxin) ↓. GenX (ZO-1 & Occ, duodenum) ↔ (ZO-1, ileum) ↑, (ZO-1, jejunum) ↓^{X}, (OCC & CL-1, jejunum & ileum) ↑, (CL-1, jejunum) ↔
30	C57BL/6J mice (*n* = 10, 5wk, 100%)		56d (PP)	Green tea extract	2% w/w diet	Permeability (FITC-Dx) ↔, (Endotoxemia) ↓. GenX (ZO-1 & OCC & CL-1, colon & ileum & jejunum) ↔. ProtX (CL-1, intestine) ↔
		HFD	56d (S+PP)	Green tea extract	2% w/w diet	Permeability (FITC-Dx, Endotoxemia) ↑^{X}.

						(ZO-1 & Occ & CL-1) ↓^{X}. GenX (ZO-1 & OCC, jejunum) ↔$^{\emptyset}$, (ZO-1, ileum) ↔$^{\emptyset}$, (CL-1, jejunum) ↓^{X}, (OCC & CL-1, ileum) ↓^{X}. ProtX (CL-1, intestine) ↓^{X}
31	C57BL/6J mice (*n* = 10, 100%)	HFD	56d (S+PP)	Green tea extract	2% w/w diet diet	Permeability (Endotoxemia) ↑^{X}. GenX (ZO-1 & Occ & CL-1, ileum & colon) ↓^{X}, (JAM-A) ↓^{X}, (JAM-A, ileum) ↔$^{\emptyset}$
32	Transgenic DQ8 mice on GFD for several generations (*n* = 5, 6-12wk)	gliadin proteins (25 mg/kg, every 2d, IGG)	15d (PP)→ 30d (PP+S)	Green Tea extract	50 mg/kg/day	Attenuated S-induced; crypt depth ↑, villus height ↓, and villus height/crypt depth ↑
33	BALB/c mice (*n* = 10, 6wk, 100%)	CTX (80 mg/kg BW/day, IPI)	3d (S) → 10d (PP)	Tea flowers extract	200 mg/kg·BW/day (IGG)	MPO ↓^{X}. GenX (CL-1 & CL-5 & OCC) ↓^{X}. Induction of repair of S-disrupted crypts and villi (jejunum)
34	C57BL/6 mice (*n* = 10, 4-5wk, 20g, 100%)	Alcohol 40% (10 mL/kg BW, OA)	Daily for 84d; mono-dose S → after 6h mono-dose PP	Fu brick tea H_2O extract	400 mg/kg BW/day	Permeability (LPS) ↑^{X}. GenX (ZO-1 & OCC) ↑, (CL)↔. ProtX (ZO-1 & OCC) ↓^{X}, OCC, ileum) ↓^{X}. Gut villi n. ↓^{X}. Gut integrity ↓^{X}
35	Sprague-Dawley rats (*n* = 8, 4wk, 100%)	HFD	84d (S+PP)	Fu brick tea (poly)phenols	100 mg/kg/day (IGG)	Permeability (LPS) ↑^{X}. ProtX & GenX (ZO-1 & OCC & CL-1) ↓^{X}. Neutral mucins ↓^{X}. GC n. ↓^{X}. Destruction of villi ↑^{X}
	Sprague-Dawley FMT rats (*n* = 8, 8wk, 100%)	HFD	84d (S+PP)	Fu brick tea (poly)phenols	100 mg/kg/day (IGG)	Permability (LPS) ↑^{X}. ProtX & GenX (ZO-1 & OCC & CL-1) ↓^{X}. Neutral mucins ↓^{X}. GC n. ↓^{X}. Destruction of villi ↑^{X}
36	C57BL/6J mice (*n* = 10/group, 7wk, 20 ± 2 g, 100%)	DSS (3.5% w/v in drinking H_2O OA)	7d (PP+S) → 5d (PP)	Aged Ripe Pu-erh Tea produced in 2006	10 mg/kg BW/day	MPO ↑^{X}. ProtX (ZO-1 & Occ & Muc2) ↓^{X}
				Aged Ripe Pu-erh Tea produced in 2010	10 mg/kg BW/day	MPO ↑^{X}. ProtX (ZO-1 & Muc2) ↓$^{\emptyset}$, (OCC) ↓^{X}
37	C57BL/6 mice (n = 7, 6wk, 20.4 ± 1 g, 100%)	HFD	105d (S+PP)	Raw Pu-erh tea, Ripened Pu-erh tea	300 and 600 mg/kg/day (IGG)	Permeability (LPS) ↑^{X}
38	C57BL/6N mice (n = 10, 8wk, 100%)		56d (PP)	Ripened Pu-erh tea extract	0.4% (w/v) in drinking H_2O	Permeability (LPS) ↔. GenX (ZO-1 & OCC, ileum) ↓

		HFD	56d (S+PP)	Ripened Pu-erh tea extract	0.1, 0.2, and 0.4% (w/v) in drinking H_2O	Permeability (LPS) ↑^{X}. GenX (ZO-1 & OCC, ileum) ↑^{X}
39	C57BL/6J mice (*n* = 10, 6wk, 16-20g, 100%)		84d (PP)	Pu-erh tea	750 mg/kg/day in drinking H_2O	Permeability (LPS) ↔. GenX (ZO-1 & OCC, ileum) ↔, (Muc2, ileum) ↑
		HFD	84d (S+PP)	Pu-erh tea	750 mg/kg/day in drinking H_2O	Permeability (LPS) ↑^{X}. GenX (ZO-1 & OCC, ileum) ↔$^{\emptyset}$. Muc2, ileum) ↓^{X}
				Tea (poly)phenols	250 mg/kg/day in drinking H_2O	Permeability (LPS) ↑^{X}. GenX (ZO-1 & OCC, ileum) ↔$^{\emptyset}$, (Muc2, ileum) ↓$^{\emptyset}$
				Oxidised tea (poly)phenols	250 mg/kg/day in drinking H_2O	Permeability (LPS) ↑^{X}. GenX (ZO-1 & OCC, ileum) ↔$^{\emptyset}$, (Muc2, ileum) ↓^{X}
40	C57BL/6N mice (*n* = 10, 8wk, 50%)	HFD	84d (S+PP)	Raw Bowl Tea (Tuocha) extract	50mg/kg/day (IGG)	Permeability (LPS) ↑^{X}. ProtX (ZO-1 small intestine) ↓$^{\emptyset}$, (OCC, small intestine) ↓^{X}. GenX (ZO-1 & OCC, small intestine) ↓^{X}
					100mg/kg/day (IGG)	Permeability (LPS) ↑^{X}. ProtX & GenX (ZO-1 & OCC, small intestine) ↓^{X}
41	Wistar rats (*n* = 6, 7wk, 100%)		22d (PP)	Tea catechin extract	0.1% drinking H_2O	Mucin content (jejunum & ileum & colon) ↔. Sialomucins/sulfomucins ↔
					0.5% drinking H_2O	Mucin content (jejunum & colon) ↔, (ileum) ↑. Sialomucins/sulfomucins ↓
Grape						
42	Caco-2		24h(PP)	Grape seed extract	50 µg/mL GAE	ProtX (OCC & CL-4) ↔
		LPS (5 µg/mL)	4h (S) → 24h (PP)	Grape seed extract	50 µg/mL GAE	ProtX (OCC & CL-4) ↓^{X}
	Weanling TOPIGS-40 piglets (*n* = 5, 21d, 9.04±0.13 kg)		30d (PP)	Grape seed meal	8% diet	ProtX (ZO-1 & OCC & CL-4) ↔. GenX (ZO-1 & OCC & CL-1 & CL-2 & CL-4 & CL-5 & CL-14 & CL-20 & CL-23 & E-cad & Muc2) ↔
		DSS (1	30d (PP+S, S Day	Grape seed meal	8% diet	ProtX (ZO-1 & OCC & CL-4) ↓^{X}. GenX

		gr/BW/day)	1-5 and 21-25)			(ZO-1 & OCC & CL-1 & CL-4 & CL-5 & CL-14 & CL-20 & CL-23 & Muc2) ↓^{X}, (CL-2) ↑^{X}, (E-cad) ↔$^{\emptyset}$
27	Caco-2		1-7d, 7d (TEER)	Grape seed extract	10 ppm	TEER TD ↑. GenX (ZO-1) ↑, (OCC & CL-2 & CL-3 & CL-15 & JAM-A) ↔
					100 ppm	TEER TD ↑. GenX (ZO-1 & OCC & JAM-A) ↑, (CL-2 & CL-3 & CL-15) ↔
43	Caco-2		24h (PP)	Grape seed extract rich in procyanidins	12.5 µg/mL	TEER ↑. ProtX (ZO-1 & OCC & CL-1) ↑.
		LPS (25 µg/mL)	24h (PP+S)	Grape seed extract rich in procyanidins	12.5 µg/mL	TEER ↓^{X}. ProtX (ZO-1 & OCC & CL-1) ↓^{X}. GenX (ZO-1) ↓^{X} Loc (ZO-1 & OCC) change^{X}
44	HT-29		14.5h (PP)	Red wine extract	200 µg/mL	ProtX (ZO-1 & CL-5) ↔, (OCC) ↑
					400 µg/mL	ProtX (ZO-1 & OCC & CL-5) ↑
			14.5h (PP, Permeability and TJs proteins). 8.5h (TJs gene)	Red wine extract	600 µg/mL	Permeability (Para) ↓. ProtX (ZO-1 & Occ & CL-5) ↑, (CL-2) ↓. GenX (ZO-1) ↑
		TNF-α (20 ng/mL) + IL-1 (10 ng /mL) + INF γ (50 ng/mL)	0.5h (PP) → 14 h (PP+S)	Red wine extract	200 µg/mL	ProtX (ZO-1 & OCC) ↓^{X}, (CL-5) ↓$^{\emptyset}$
					400 µg/mL	ProtX (ZO-1 & OCC & CL-5) ↓^{X}
			0.5h (PP) → 14 h (PP+S, Permeability and TJs proteins). 30min (PP) → 8 h (TJs gene).	Red wine extract	600 µg/mL	Permeability (Para) ↑^{X}. ProtX (ZO-1 & OCC & CL-2 & CL-5) ↓^{X}. GenX (ZO-1 & OCC & CL-5) ↓^{X}
45	Caco-2		4h (PP)	*In vitro* colonic digested grape pomace extract	500 µL (1:40 dil)	Permeability (Para) ↑. GenX (ZO-1 & OCC) ↔
				In vitro small intestine digested grape pomace extract	500 µL (1:40 dil)	Permeability (Para) ↓. GenX (ZO-1 & OCC) ↔
46	Caco-2		16h (PP)	*In vitro* colonic	1:40 dil	Permeability (Para) ↔. ProtX (ZO-1 & OCC)

				digested wine		↔
			4h (PP)	*In vitro* small intestine digested wine	1:40 dil	Permeability (Para) ↔. ProtX (ZO-1 & OCC) ↔
47	IEC-6		24h (PP)	Grape seed PCs extract	10 μg/mL	ProtX & GenX (ZO-1 & OCC) ↑
		H_2O_2 (500μM)	24h (PP) → 4h (PP+S)	Grape seed PCs extract	10 μg/mL	ProtX & GenX (ZO-1 & OCC) ↓^{X}
	Sprague Dawley rats recently weaned (*n* = 24, 21d, 28.8 ± 1.7 g, 100%)	Weaning	29d (diet with zinc 105 mg/kg) + PP)	Grape seed procyanidins extract	250 mg/kg	Permeability (L/M) ↓. ProtX & GenX (ZO-1 & OCC, intestine) ↑
48	Caco-2	IL-6+IL-1β (10ng/mL)	48h (PP+S, TEER), 72h (PP+S) (Permeability)	Grape seed extract	3 μg/mL	TEER ↓^{X}. Permeability ↑^{X}. ProtX (ZO-1) ↔^{Ø}, (CL-2) ↑^{X}, (CL-3 & CL-7) ↓^{X}
	Sprague-Dawley rats (*n* = 6-7, 7wk, ~300g, 100%)	WAS (1h)	7d (PP) → 3d (PP + S) → 1d (PP)	Grape seed extract	100 mg/kg/day (IGG)	Permeability ↑^{X}. ProtX (ZO-1) ↔^{Ø}, (CL-2) ↑^{X}, (CL-3) ↓^{Ø}, (CL-7) ↑
		Sham (1h)	7d (PP) → 3d (PP + S) → 1d (PP)	Grape seed extract	100 mg/kg/day (IGG)	Permeability ↔^{Ø}. ProtX (ZO-1 & CL-7) ↔^{Ø}, (CL-2) ↑^{X}, (CL-3) ↓^{X}
49	Caco-2	*L. monocytogenes* ILSI9 (MOI 25:1)	1h (PP+S)	Wine Pomace Product	40 g/L	GenX (OCC) ↓^{X}, (CL & E-cad) ↔^{Ø}
		L. monocytogenes ILSI17, or ILSI18, or ILSI19, or S11 (MOI 25:1)	1h (PP+S)	Wine Pomace Product	40 g/L	GenX (OCC & E-cad) ↓^{X}, (CL) ↔^{Ø}
50	C57BL/6 mice (6-12wk) *ex vivo* ileal crypts isolated from ileocecal		72h (PP)	Grape seed proanthocyanidin extract	5 mg/L	GenX (Muc2) ↑

	junction and grown as organoids					
51	Broiler Cobb chicks (*n* = 15, 100%)		21d (PP)	Grape extract	2.5 g/kg diet/day	Mucus content (jejunum) ↔. Sialic acid content in ileal digesta ↔. Villus height (jejunum) ↔. Crypt depth (jejunum) ↔. GCs n. (jejunum) ↔
					5 g/kg diet/day	Mucus content (jejunum) ↔. Villus height (jejunum) ↔. Crypt depth (jejunum) ↔. GCs n. (jejunum) ↔
52	C57BL/6N mice post-weaning (*n* = 6, 3wk, 100%)		14d (PP)	Grape (poly)phenols pomace extract	200 mg/kg BW/day	GenX (OCC & JAM-A & CL-2 & CL-3 & Muc1 & Muc2) ↑, (ZO-1 & ZO-2 & CL-1) ↔. Mucosa thickness ↑. Mucosa content ↑. Muc2 density ↑. Crypth depth ↑. GC n. ↑
	C57BL/6N mice (*n* = 6, 6wk, 100%)		14d (PP)	Grape (poly)phenols pomace extract	200 mg/kg BW/day	GenX (CL-3) ↑, (ZO-1 & ZO-2 & Occ & Jam-A & CL-1 & CL-2 & Muc2) ↔. Mucosa thickness ↔. Mucosa content ↔. Muc2 density ↔. Crypth depth ↔. GC n. ↔
53	Crossed bread weaned piglets (*n* = 30)		28d (PP)	Grape seed proanthocyanidins	250 mg/kg/day	ProtX (ZO-1 & CL-1, jejunum & colon) ↔, (OCC, jejunum & colon) ↑. Villus height (jejunum & ileum) ↑. Crypt depth (jejunum & ileum) ↓
		Antibiotic treatment; colistin sulphate (20 mg/kg)	28d (PP+S)	Grape seed proanthocyanidins	250 mg/kg/day	Permeability (L/M) ↓. Crypt depth (jejunum & ileum) ↓. ProtX (ZO1 & CL-1, jejunum & colon) ↔, (OCC, jejunum & colon) ↑. Villus height (jejunum & ileum) ↑. Crypt depth (jejunum & ileum) ↓
54	Crossbred piglets weaned at 21d (*n* = 10 (3 replicates), 6.52 ± 0.18 kg)		6d (PP) → 7-14d (PP+chromic oxide (3 g/kg diet)) → 15-20d (PP) → 21-28d (PP+chromic oxide (3 g/kg diet))	Grape seed procyanidins extract	50 mg/kg	Permeability (Endotoxin at day 14 & 28) ↔
				Grape seed procyanidins extract	100 and 150 mg/kg	Permeability (Endotoxin at day 14 & 28) ↓

55	Wistar Furth rats (*n* = 8, 6-7wk, 100%)		21d (PP) → after 24h (PP via IGG) & end study after 8h	Grape seed extract	~100mg/kg/day /100g BW in drinking H_2O + ~250 mg/kg PP (IGG)	Permeability (Endotoxemia) ↔. Faecal calprotectin ↓. GenX (ZO-1 & ZO-2 & CL-1, cecum & proximal colon & distal colon) ↔, (OCC, cecum) ↓, (OCC, proximal colon) ↑, (OCC, distal colon) ↔
56	Rainbow trouts (*n* = 9, ~1.3g)		60d (PP)	Grape seed extract	100 mg/kg diet	Acidic mucin ↔. Neutral mucin ↔. Mixed mucin ↔ GC density (middle & posterior intestine) ↔. Villus density, width, height (anterior, middle, and posterior intestine) ↔. GC density (anterior intestine) ↑
					200 mg/kg diet	Acidic mucin ↔. Neutral mucin ↔. Mixed mucin ↔. GC density (middle & posterior intestine) ↔. Villus width and density (anterior and middle intestine) ↔. Villus density (posterior intestine) ↔. GC density (anterior intestine) ↑. Villus height (anterior, middle & posterior intestine). Villus width (posterior intestine) ↑
57	WT mice (*n* = 9)		112d (PP)	Grape seed extract	1% g/g dry diet	MPO ↔. GC density ↑
	IL10KO mice (n = 11)	IL10KO	112d (PP)	Grape seed extract	1% g/g dry diet	MPO $↑^{X}$. GC density ↑
58	IL10KO mice (*n* = 10, 6wk, 0%)	IL10KO	84d (PP)	Grape seed extract (Gravinol-S)	0.1% v/v H_2O	Mucus thickness (jejunum) ↑. Villus length (jejunum) ↑. Crypt depth (jejunum) ↔. GC/villus ↑
59	IL10KO mice (*n* = 10, 6wk, 0%)	IL10KO	84d (PP)	Grape seed extract (Gravinol-S™)	0.1% w/v drinking H_2O	Permeability ↓. β-catenin (content, nuclear accumulation, and phosphorylated form) ↓. GenX (Muc1) ↔, (Muc2 & Muc3) ↑. GC density ↑
60	Wistar rats (*n* = 8, 3wk, 80-100 g, 100%)	HFD	90d (S+PP, PP for 6 times/wk)	Grape seed procyanidin extract	200 mg/kg BW/day	Permeability (LPS & D-lactate) $↑^{X}$. GenX (ZO-1 & OCC) $↓^{X}$, (ZO-1 & Occ, ileum) ↑. Crypt depth $↓^{X}$. Crypt depth (ileum) $↓^{ø}$. Villus length (ileum) ↔
61	C57BL/6J mice	HFD	56d (S+PP)	Grape pomace extract	8.2 g/kg diet	GenX (ZO-1 & OCC & CL-3 & Muc2) $↔^{ø}$

	(*n* = 14, 9wk, 100%)					
62	C57BL/6J mice (*n* = 15, 5wk, 10-20 g, 100%)	HFD	91d (S+PP)	Grape polyphenols extract	1% diet	Permeability (LPS) ↓. GenX (ZO-1, jejunum) ↔, (OCC) ↑
63	C57BL/6J mice (*n* = 10, 4wk, 100%)	HFD	112d (S+PP)	Table grapes PP rich fraction extract	5% w/w diet	Permeability (LPS) ↑[Ø]. MPO ↑[X]. ProtX (ZO-1, ileum) ↓[X]. Loc (ZO-1, ileum) change[X]
				Table grapes PP poor fraction extract	5% w/w diet	Permeability (LPS) ↑[X]. MPO ↑[X]. ProtX (ZO-1, ileum) ↓[X]. Loc (ZO-1, ileum) change[X]
				Table grape PP rich fraction extract with table grape PP poor fraction extract	5% w/w diet	Permeability (LPS) ↑[X]. MPO ↑[X]. ProtX (ZO-1, ileum) ↓[Ø]. Loc (ZO-1, ileum) change[X]
				Lyophilised table grapes	5% w/w diet	Permeability (LPS) ↑[Ø]. MPO ↑[X]. ProtX (ZO-1, ileum) ↓[Ø]. Loc (ZO-1, ileum) change[X]
64	C57BL/6J mice (*n* = 10, 4wk, 100%)	HFD + sugar (3% w/w diet)	70d (S+PP)	Powdered grape	3% w/w diet	ProtX (ZO-1, ileum) ↑, (OCC, CL-1, ileum) ↓[Ø]. Loc (ZO-1, ileum) change[Ø]
					5% w/w diet	ProtX (ZO-1 & OCC & CL-1, ileum) ↔. Loc (ZO-1, ileum) change[Ø]
65	Wistar rats (*n* = 10, 47wk, 240-270g, 0%)	CAF	105d (S) → 14d (S+PP)	Grape seed proanthocyanidins extract	100 mg/kg BW/day	TEER (duodenum) ↓[Ø], (ileum & colon) ↓[X]. Permeability (OVA & LPS) ↑[X]. MPO ↑[X]. GenX (ZO-1 & CL-2 & JAM-A, ileum) ↔[Ø], (CL-1, ileum) ↓[X]
					500 mg/kg BW/day	TEER (duodenum) ↓[Ø], (ileum & colon) ↓[X]. Permeability (OVA) ↑[Ø], (LPS) ↑[X]. MPO ↑[X]. GenX (ZO-1 & CL-2 & JAM-A, ileum) ↔[Ø], (CL-1, ileum) ↓[X]
66	Wistar rats (*n* = 6/group, 36wk, 0%)	CAF	105d (S) → 21 (S+PP)	Grape seed procyanidins extract	5 and 50 mg/kg BW/day	Permeability (LPS) ↔[Ø]. MPO ↑[X]. GenX (ZO-1, ileum) ↓[X], (OCC & CL-1 & JAM-A, ileum) ↔[Ø]
					25 mg/kg BW/day	Permeability (LPS) ↔[Ø]. MPO ↑[X]. GenX (ZO-1, ileum) ↓[Ø], (OCC & CL-1 & JAM-A, ileum) ↔[Ø]

67	Wistar rats (*n* = 10, 47wk, 240-270g, 0%)	CAF	119d (S+PP)	Grape seed extract	100 mg/kg BW/day	Villous height, villus/crypt ratio, GC n. (duodenum, colon); ↔$^{\emptyset}$. Villous height, villus/crypt ratio; (duodenum) ↑$^{\emptyset}$
					500 mg/kg BW/day	Villous height, villus/crypt ratio; ↔$^{\emptyset}$. Villous height, villus/crypt ratio; (duodenum) ↑$^{\emptyset}$. GC n. (duodenum); ↑^{X}
			119d (S+PP, PP every other wk)	Grape seed extract	500 mg/kg BW/day	GC n. (duodenum & ileum & colon) ↔$^{\emptyset}$
68	Wistar rats (*n* = 10, 7wk, 240-270g, 0%)	CAF	10d (PP) → 119d (S)	Grape seed proanthocyanidins extract	500 mg/kg BW/day	TEER (duodenum & colon) ↓^{X}, (ileum) ↓$^{\emptyset}$. Permeability ↔$^{\emptyset}$, (OVA & LPS, wk 12 & 17 of CAF) ↑^{X}, (LPS, wk 8 & 12 of CAF) ↑$^{\emptyset}$. GenX (ZO-1 & OCC & CL-2 & CL-3 & JAM-A, ileum) ↔$^{\emptyset}$, (CL-1, ileum) ↓$^{\emptyset}$
			119d (S+P, PP daily every other wk)	Grape seed proanthocyanidins extract	500 mg/kg BW/day	TEER ↓$^{\emptyset}$, (duodenum & ileum) ↓^{X}. Permeability ↔$^{\emptyset}$, (OVA, wk 12 & 17 of CAF) ↑^{X}, (LPS, wk 17 of CAF) ↑^{X}, (LPS, wk 8 & 12 of CAF) ↑$^{\emptyset}$. GenX (ZO-1 & OCC & CL-2 & CL-3 & JAM-A, ileum) ↔, (CL-1, ileum) ↓^{X}
69	C57BL/6J mice (*n* = 8, 6-7wk, 20±2 g, 100%)	DSS (2.5% w/v in drinking H_2O)	14d (PP) → 7d (PP+S)	Grape seed PCs extract	50 mg/kg/day	GenX (ZO-1 & OCC & CL-1) ↓^{X}
70	Wistar rats (*n* = 8, adults, 200 ± 20 g, 100%)	TNBS (10 mg/day)	15d (PP) → 1d (PP+S) + 7d (PP)	Grape Peel Powder	40 mg/kg BW/day	GenX (ZO-1) ↓^{X}, (CL-2) ↑$^{\emptyset}$, (OCC) ↔$^{\emptyset}$. Lesion area, macroscopic damage ↑$^{\emptyset}$. Microscopic damage ↔$^{\emptyset}$
				Extractable grape peel powder PP-rich fraction	40 mg/kg BW/day	GenX (ZO-1) ↓^{X}, (CL-2) ↑^{X}, (OCC) ↔$^{\emptyset}$. Lesion area, macroscopic damage ↑. Microscopic damage ↔$^{\emptyset}$
				Non-extractable grape peel powder PP-rich fraction	40 mg/kg BW/day	GenX (ZO-1) ↓^{X}, (CL-2) ↑^{X}, (OCC) ↔$^{\emptyset}$. Lesion area ↑^{X}. Macroscopic damage ↑$^{\emptyset}$. Microscopic damage ↔$^{\emptyset}$
32	Transgenic DQ8	gliadin	15d (PP) → 30d	Grape seed oligomeric	50 mg/kg/day	Attenuated stress induced crypt depth ↑,

	mice on GFD for several generations (*n* = 5, 6-12wk)	proteins (25 mg/kg, every 2d, IG)	(PP+S)	procyanidins		villus height ↓, and villus height/crypt depth ↑
71	Human proximal colon tissues from colectomised patients (*n* = 27, BMI = 27.3±0.8 kg/m^2, 48.1%)	DSS (12% w/v in KRB buffer)	0.5h (PP) → 0-1h (S)	Grape seed proanthocyanidin extract (in KRB buffer)	50, 200 µg/mL	TEER ↓^{X}. Permeability (FD4) ↓
	Human distal colon tissues from colectomised patients (*n* = 34, BMI = 28.1±1.1 kg/m^2, 60%)	DSS (12% w/v in KRB buffer)	0.5h (PP) →0-1h (S)	Grape seed proanthocyanidin extract (in KRB buffer)	50, 200 µg/mL	TEER ↓^{Ø}. Permeability (FD4) ↔
Other						
27	Caco-2		1-7d (TJs), 7d (TEER)	Chestnut extract	10 ppm	TEER ↔. GenX (ZO-1 & OCC & CL-2 & CL-3 & CL-15 & JAM-A) ↔
					100 ppm	TEER TD ↓. GenX (ZO-1 & OCC & CL-3 & CL-15 & JAM-A) ↔, (CL-2) ↓
72	C57BL/6 mice with HFD and streptozotocin induced diabetes (*n* = 7, 18 ± 2 g, 100%)	HFD	28d (PP+S, HFD)	Peanut skin procyanidins	75 mg/kg BW/day (IGG)	Permeability (LPS) ↑^{X}. MPO ↑^{X}. ProtX (ZO-1) ↓^{X}, (OCC & CL-1) ↓^{Ø}. Villi height ↓^{Ø}. Crypt depth ↔^{Ø}
					150 mg/kg BW/day (IGG)	Permeability (LPS) ↑^{X}. MPO ↑^{X}. ProtX (ZO-1) ↓^{X}, (OCC & CL-1) ↓^{Ø}. Villi height ↓^{X}. Crypt depth ↔^{Ø}
					300 mg/kg BW/day (IGG)	Permeability (LPS) ↑^{X}. MPO ↑^{X}. ProtX (ZO-1 & OCC & CL-1) ↓^{Ø}. Villi height ↓^{X}. Crypt depth ↔^{Ø}
73	Caco-2		25h (Permeability), 0.5-2.5h (TEER)	Polymeric proanthocyanidins fraction from Sicilian	12 mg cyanidin equivalent/mL	TEER ↑. Permeability (Para) ↔

				pistachio nut, Hydrophilic extract from Sicilian pistachio nut rich in proanthocyanidins		
		IL-1β (25 ng/mL)	1h (PP) → 24h (S+PP)	Polymeric proanthocyanidins fraction from Sicilian pistachio nut, Hydrophilic extract from Sicilian pistachio nut rich in proanthocyanidins	12 mg cyanidin equivalent/mL	Permeability (Para) ↑^{X}
Monomers, Oligomers, and Polymers						
74	Caco-2		0-3h (PP)	(–)-Epicatechin	100 µM	TEER ↔
		Theobromine (100 µM)*	0-3h (PP)	(–)-Epicatechin	100 µM	TEER ↔$^{\emptyset}$
		Lauric acid (3 mM)	0-3h (PP+S)	(–)-Epicatechin	100 µM	TEER ↓$^{\emptyset}$
75	Caco-2	TNFα (20 ng/ml)	6h (PP) → 48h (PP+S, with replacement of PP & S after 24h only in TEER and Para experiments)	(–)-Epicatechin	1 µM	TEER ↓^{X}. Permeability (Para) ↑^{X}. ProtX (ZO-1) ↓^{X}, (OCC & CL-2) ↔$^{\emptyset}$. Loc (ZO-1) change^{X}
76	Caco-2	DCA (100µM)	2h and 4h (PP+S)	(–)-Epicatechin	1 µM	Permeability (Para) TD ↑^{X}
					10 µM	Permeability (Para) ↑^{X}
			0-4h (PP+S)	(–)-Epicatechin	5 µM	Permeability (Para) ↑^{X}. ProtX (ZO-1 & OCC) ↓^{X}
77	Isolated vascular perfused colon from Wistar rats		10 min equilibration → 0.5h PP	(–)-Epicatechin	up to 20 mM	ProtX (Mucins) ↔

			stimulation			
78	Caco-2	IFN-γ (10 ng/ml) + TNFα (5 ng/ml)	24h (S, IFN-γ) → 0.5h (PP) → 6h (PP+S, TNFα)	(–)-Epicatechin	1 µM	TEER ↓^{X}. Permeability (Para) ↑^{X}
	C57BL/6J mice (*n* = 9-10, 20–25 g, 100%)		105d (PP)	(–)-Epicatechin	20 mg/kg BW	Permeability (FITC-Dx & LPS) ↔, (GLP-2) ↑. ProtX (ZO-1 & OCC & CL-1, ileum) ↔
		HFD	105d (S+PP)	(–)-Epicatechin	2 mg/kg BW	Permeability (FITC-Dx) ↔, (LPS) ↑$^{\emptyset}$
					10 mg/kg BW	Permeability (FITC-Dx) ↔, (LPS) ↑^{X}
					20 mg/kg BW	Permeability (FITC-Dx) ↔, (LPS) ↑^{X}, (GLP-2) ↑. ProtX (ZO-1 & OCC & CL-1) ↓^{X}
79	T84		4h (PP, TEER), 4-24h (PP, TJs)	(–)-Epicatechin	10 µM	TEER ↑. GenX (ZO-1) TD ↑, (OCC & CL-4) ↔
				(+)-Catechin	10 µM	TEER ↑. GenX (ZO-1 & OCC & CL-4) TD ↑
		Caprylic acid (10 mM)	10min (S) → 4h (PP+S)	(–)-Epicatechin	10 µM	TEER ↔
				(+)-Catechin	10 µM	TEER ↓^{X}
80	T84	Sodium caprate (10mM)	10min (S) → 0.6-4h (PP)	(–)-Epicatechin	20 µM	TEER ↓^{X}
				(+)-Catechin	20 µM	TEER ↓^{X}
81	Caco-2 + HT-29 MTX		0-96h (PP, TEER), 24 and 96h (PP, TJs)	(+)-Catechin, Procyanidin B2	50 µM	TEER ↔. ProtX (ZO-1) ↓, (OCC & CL-7) ↑
		MCM	24h (PP) → 0-96h (PP+S, TEER)	(+)-Catechin	50 µM	TEER ↓$^{\emptyset}$. ProtX (ZO-1 & OCC) ↓$^{\emptyset}$, (CL-7) ↑$^{\emptyset}$
				Procyanidin B2		TEER ↓$^{\emptyset}$. ProtX (ZO-1) ↓$^{\emptyset}$, (ZO-1) ↓^{X}, (CL-7) ↑$^{\emptyset}$
		MCM+	24h (PP) → 24-72h (PP+S, TEER), 24-96h (PP+S, TJs)	(+)-Catechin, Procyanidin B2	50 µM	TEER ↓$^{\emptyset}$

31	C57BL/6J mice (*n* = 10, 100%)	HFD	56d (S+PP)	Catechin, EGCG	0.3% w/w diet	GenX (ZO-1 & OCC & CL-1, ileum & colon) ↓X, (JAM-A, ileum) ↔∅, (JAM-A) ↓∅
82	Caco-2	CML (0.5mM)	24h (PP+S)	(+)-Catechin	20 µM, 50µM	ProtX (ZO-1) ↓X
83	C57BL/6 J mice (*n* = 8, 7-8wk, 0%)	DSS (2.5% in drinking H_2O)	7d (S) → 3d (PP+S)	EGCG	100uL PBS with 50mg/kg BW/day of PP	MPO ↑X. ProtX (TJs) ↓X. Mucosal damage ↑X. Mucus thickness ↓X. Disruption brush border ↓X
					100uL PBS with 50mg/kg BW/day of PP (RA)	MPO ↑∅. ProtX (TJs) ↓∅. Mucosal damage ↑∅. Mucus thickness ↓∅. Disruption brush border ↓∅
84	Caco-2	Indomethacin (250 µM)	0-1.7h (PP+S)	EGCG	218 µM	TEER ↓X. Permeability ↑X
85	Caco-2		48h (PP)	EGCG	50 µM	TEER ↔
		IL-1β (5 ng/mL) + TNF-α (50 ng/mL) + IFN-γ (50 ng/mL) + LPS (10 µg/mL)	48h (PP+S)	EGCG	50 µM	TEER ↔. GenX (OCC) ↔
86	T84		48h (PP)	EGCG	100 µM	TEER ↔. Permeability (Trans) ↔
		IFN-γ (20 ng/ml)	48h (PP+S)	EGCG	100 µM	TEER ↓X. Permeability (Trans) ↑X
		EPEC (10^7 organisms/monolayer), or IL-4 (20 ng/ml)	24h (PP+S)	EGCG	100 µM	TEER ↓∅
87	IPEC-J2		0-24h (TEER),	EGCG	50 µM	TEER ↔. Permeability ↔

			24h (Permeability)			
32	Transgenic DQ8 mice on GFD for several generations (*n* = 5, 6-12wk)	Indomethacin + gliadin	15d (PP+S)	EGCG	25 mg/kg/day	Villi height/crypt depth ↓[ø]
					50 and 100 mg/kg/day	Villi height/crypt depth ↓[X]
		Gliadin proteins (25 mg/kg, every 2d, IGG)	15d (PP)→ 30d (PP+S)	EGCG	50mg/kg/day	Attenuated S-induced; Crypt depth ↑, Villus height ↓, and Villus height/crypt depth ↑
88	Swiss albino mice (*n* = 5, 18 months, 40-50g, 100%) middle-aged mice	DSS (3.5% (w/v) in drinking H_2O)	30d (ND+PP) → 7d (PP+S) → 2d (PP)	EGCG	100 mg/kg BW/day	GenX (ZO-1 & OCC & Muc2) ↓[X]
89	ICR mice		5d (PBS injection) → 25d (PP)	EGCG	40mg/kg/day	Permeability (FITC-Dx) ↔. ProtX (ZO-1 & OCC & CL-1) ↔. Villi height (intestine) ↔. Crypt depth (intestine) ↔
		CTX (50mg/kg/day, injection)	5d (S) → 25d (PP)	EGCG	20mg/kg/day	Villi height (intestine) ↓[ø]. Crypt depth (intestine) ↓[ø]
				EGCG	40mg/kg/day	Permeability (FITC-Dx) ↑[X]. ProtX (ZO-1 & OCC & CL-1, small intestine) ↓[X]. Villi height (intestine) ↓[X]. Crypt depth (intestine) ↓[X]
90	Caco-2 + HT29-MTX		48h (PP)	(–)-ECG	10 µM	ProtX (Muc2) ↔. GenX (Muc2 & Muc3 & Muc13) ↔, (Muc17) ↑
91	Caco-2		3h	(–)-Epicatechin, ECG, EGC, EGCG	10 µM	Permeability ↔
				Theaflavin-3′-*O*-gallate	5 µM	Permeability (Para) ↓
			24h	Theaflavin, Theaflavin-3′-*O*-gallate, Theaflavin-3-*O*-gallate Theaflavin-3,3′-*O*-digallate	20 µM	Permeability (Para) ↓
			24h (TEER), 3h-24h	Theaflavin-3′-*O*-gallate	10 µM	TEER ↑. Permeability (Para) ↓. ProtX & GenX (ZO-1 & OCC & CL-1) ↑, (CL-3 &

			(Permeability), 1h and 3h (TJs)			CL-4 & ZO-2 & JAM-1) ↔
					20 µM	TEER ↑. Permeability (Para) ↓
					50 µM	TEER ↑
		GF109203X (10 µM)	3h (PP+S)	Theaflavin-3′-*O*-gallate	10 µM	Permeability (Para) ↓
		Compound C (10 µM)	3h (PP+S)	Theaflavin-3′-*O*-gallate	10 µM	Permebaility (Para) ↔
92	Caco-2		0.5h (PP)	Theasinesins A, Theasinesins B	500 µM	Permeability ↓
93	Lohman laying hens (*n* = 40, 25wk, 0%)		84d (PP)	Theabrownin	100 and 200 mg/kg	GenX (ZO-1 & CL-1 & Muc2, jejunum) ↑, (ZO-2 & CL-2 & OCC, jejunum) ↔
					400 mg/kg	GenX (ZO-1 & ZO-2 & CL-1 & CL-2 & OCC & Muc2, jejunum) ↔
94	Caco-2	ACR (2 mM)	6h (PP) → 24h (PP+S)	Procyanidin A1, *in vitro* digested procyanidin A1	1, 2, and 5 µM	TEER ↓^{X}. Permeability (Para) ↑^{X}. ProtX (ZO-1 & OCC & CL1) ↓^{X}
		ACR (2 mM) + ML-7 (2 µM)	1h (S, ML-7) → 6h (PP) → 24h (PP+S, ACR)	Procyanidin A1, i*n vitro* digested procyanidin A1	5 µM	TEER ↓^{X}. Permeability (Para) ↑^{X}
Simple phenolics						
95	Caco-2		4-72h (PP)	3,4-Dihydroxybenzoic acid	200µM	TEER TD ↑
				2,4,6-Trihydroxybenzoic acid	200µM	TEER TD ↓
96	Caco-2	LPS (100µg/mL)	24h (PP+S)	3,4-Dihydroxybenzoic acid	0.5 mmol/L	ProtX (ZO-1 & Muc2) ↓^{X}
				Hippuric acid	0.5 mmol/L	ProtX (ZO-1) ↓^{X}, (Muc2) ↓$^{\emptyset}$
				4-Hydroxy-3-methoxybenzoic acid	0.5 mmol/L	ProtX (ZO-1 & Muc2) ↓$^{\emptyset}$
14	Caco-2	TNF-α (50 ng/mL) + IFN-γ (50 ng/mL) + IL-	24h (PP+S)	2,3-Dihydroxybenzoic acid, 2-Hydroxy-4-Methoxy benzoic acid, Phenylacetic acid, 3-	100 µM	TEER ↓$^{\emptyset}$

		1β (25 ng/mL) + LPS (1 mg/mL)		Hydroxy-4-methoxybenzoic acid, 2,4,6-Trihydroxybenzaldehyde, 3,4-Dihydroxybenzoic acid		
45	Caco-2		16h (PP)	3′,4′-dihydroxyphenylacetic acid	200 μM	Permeability (Para) ↓. GenX (ZO-1 & OCC) ↔
46	Caco-2		16h (PP)	3′,4′-dihydroxyphenylacetic acid	200 μM	Permeability (Para) ↔. GenX (ZO-1 & OCC) ↔
97	Weaned piglets (*n* = 6, 21 ± 1d, 6.7 ± 0.4kg)		14d (PP)	Benzoic acid	2 g/kg diet	GenX (ZO-1 & OCC, jejunum) ↑. Villus height (jejunum) ↑. Crypt depth (jejunum) ↓
					5 g/kg diet	GenX (ZO-1, jejunum) ↔, (OCC, jejunum) ↑. Villus height (jejunum) ↔. Crypt depth (jejunum) ↓
			42d (PP)	Benzoic acid	2 g/kg diet	GenX (ZO-1 & OCC, jejunum) ↑. Villus height (jejunum) ↑. Crypt depth (jejunum) ↔
					5 g/kg diet	GenX (ZO-1 & OCC, jejunum) ↑. Villus height (jejunum) ↔. Crypt depth (jejunum) ↔
98	Caco-2	TNF-α (10 ng/mL)	24h (PP+S)	4-Hydroxybenzoic acid	3, 10, and 30 μM	ProtX & GenX (OCC & E-cad) ↓^{X}
		TNF-α (10 ng/mL) + PHTPP (0.1μM)	24h (PP+S)	4-Hydroxybenzoic acid	30 μM	ProtX (OCC & E-cad) ↓$^{\emptyset}$. GenX (OCC) ↓^{X}, (E-cad) ↓$^{\emptyset}$
	C57BL/6 mice (*n* = 8, 8wk, 0%)	DSS (2.5% in drinking H_2O)	7d (PP+S) → 3d (PP)	4-Hydroxybenzoic acid	10mg/kg/day	MPO ↑$^{\emptyset}$. ProtX (OCC & E-cad) ↓^{X}. GenX (OCC & E-cad) ↓$^{\emptyset}$. Colonic tissue damage ↑^{X}
					20mg/kg/day	MPO ↑$^{\emptyset}$. Prot X (OCC & E-cad) ↓^{X}. GenX (OCC) ↓^{X}, (E-cad) ↓$^{\emptyset}$. Colonic tissue damage ↑^{X}

				4-Hydroxybenzoic acid	40mg/kg/day	MPO ↑X. ProtX & GenX (OCC & E-cad) ↓X. Colonic tissue damage; ↑X
		DSS (2.5% in drinking H_2O), PHTPP (1mg/kg/day, IPI)	10d (PP+S, DSS and PHTPP) → 3d (PP+S, PHTPP)	4-Hydroxybenzoic acid	40mg/kg/day	MPO ↑ø. ProtX & GenX (OCC & E-cad) ↓ø. Colonic tissue damage ↑ø
99	Duroc × (Yorkshire × Landrace) pigs (*n* = 10, 18.7 ± 0.2kg)		14d (PP)	Benzoic acid	5 g/kg diet	ProtX & GenX (GLP-2, jejunum) ↑. Villus height (jejunum) ↔. Crypt depth (jejunum) ↓
79	T84		4h (TEER), 4-24h (TJs)	3′,4′-dihydroxyphenylacetic acid	20 µM	TEER ↑. GenX (ZO-1 & OCC & CL-4) ↔
				3-(3,4-Dihydroxyphenyl)propanoic acid, Benzene-1,3,5-triol	20 µM	TEER ↑. GenX (ZO-1 & OCC & CL-4) TD ↑
				3-(4′-hydroxyphenyl)propanoic acid	20 µM	TEER ↑. GenX (ZO-1) TD ↑, (OCC) TD ↓, (CL-4) ↔
		Caprylic acid (10 mM)	10min (S) → 4h (PP+S)	3-(3,4-Dihydroxyphenyl)propanoic acid, 3′,4′-dihydroxyphenylacetic acid, 1,3,5-Trihydroxybenzene	20 µM	TEER ↓X
				3-(4-hydroxyphenyl)propanoic acid	20 µM	TEER ↓ø
100	IPEC-J2		5h (PP)	3,4,5-Trihydroxybenzoic acid	100 µg/L	ProtX (ZO-1 & OCC) ↔
39	C57BL/6J mice	HFD	84d (S+PP)	3,4,5-	50 mg/kg/day	Permeability (LPS) ↑ø

	(*n* = 10, 6wk, 16-20g, 100%)			Trihydroxybenzoic acid		
101	Wistar rats (*n* = 6, 6wk, 115-160g, 0%)	DMH (40 mg/kg BW + 1mM EDTA as vehicle, SI)	14d (PP) & on day 14 (PP+S)	3,4,5-Trihydroxybenzoic acid	25 and 50 mg/kg BW/day	Sialomucins relative abundance and destruction of mucosal region: ↑X. GC disintegration: ↑X
102	IPEC-J2		24h (PP)	3,4,5-Trihydroxybenzoic acid	5 and 25 µmol/L	TEER ↔. ProtX & GenX (ZO-1 & OCC & CL-1) ↔
					50 µmol/L	TEER ↓. ProtX (ZO-1 & OCC) ↔, (CL-1) ↓. GenX (ZO-1 & Occ & CL-1) ↔
	Swiss Large White pigs (0%) ex vivo pig jejunum		0.5h (PP)	3,4,5-Trihydroxybenzoic acid	5 µmol/L	TEER ↔. ProtX (ZO-1 & OCC) ↔, (CL-1) ↓
					25 µmol/L	TEER ↔. ProtX (ZO-1 & CL-1) ↓, (OCC) ↔
					50 µmol/L	TEER ↔. ProtX (ZO-1 & OCC & CL-1) ↓

ACR, acrylamide; AMVN, 2,2′-azobis(2,4-dimethylvaleronitrile); BW, body weight; CAF, cafeteria diet; CL, claudin; CML, Nε-carboxymethyl lysine; Compound C, 5′-AMP-activated protein kinase-inhibition; CTX, Cyclophosphamide; d, day(s); DCA, deoxycholic acid; DMH, 1,2-dimethylhydrazine; DSS, dextran sulphate sodium; E-cad, E-cadherin; ECG, epicatechin gallate; EGC, epigallocatechin; EDTA, Ethylenediaminetetraacetic acid; EGCG, epigallocatechin gallate; EEN, elemental enteral nutrition; EPEC, Enteropathogenic Escherichia coli; EtOH, ethanol; FD4; fluorescently-labelled dextran; FITC-Dx, Fluorescein Isothiocyanate-Dextran; FMT, mice that received oral supplementation of the faecal bacteria collected from mice previously supplemented intragastrically with 100 mg/kg/day for 4 weeks with high-fat diet; GAE, gallic acid equivalents; GC, goblet cells; GF109203X, not-specific protein kinase C inhibitor; GLP-2, Glucagon-Like Peptide-2; H_2O, water; HFD, high-fat diet (≥ 44% caloric content from fat); HFHS, high fat high sugar diet; IFN-γ, cytokine interferon- γ; IL-6, cytokine interleukin 6; IL-1β, cytokine interleukin-1β; IGG, intragastric administration; IL10KO, interleukin-10 knockout; IPI, intraperitoneal injection; KRB, Krebs–Ringer bicarbonate buffer; LFD, low fat diet; LPS, lipopolysaccharide; LY294002, phosphoinositide-3-kinase–protein kinase B/Akt inhibitor; MCM, Macrophage Conditioned Medium; MCM+, medium of activated macrophages; ML-385, Nrf2-specific inhibitor; ML-7, myosin light chain kinase-inhibitor; MPO, myeloperoxidase; MOI, multiplicity of infection; n., number; OCC, occludin; OVA, ovalbumin; Para, paracellular permeability; PHTPP, estrogen receptor (Erβ) selective antagonist; PP, (poly)phenolic source; RA, rectal administration; S, stressor; SI, subcutaneous injection; TD, time-dependent effect; TEER, transepithelial electrical resistance; TLR4m, Toll-like receptor 4 mutated; TJ, tight junction; TNBS, 2,4,6 trinitrobenzene sulfonic acid; TNF-α, Tumor Necrosis Factor Alpha; Tr+ : transfected with Lentivirus-miR-200c-3p; Tr-, transfected with Lentivirus-miR-200c-3p-sponge; Trans, transepithelial permeability; WAS, water avoidance stress; wk, week(s); WT, wild-type; ZO, zonula occludens; ZnPP, protease inhibitor.

Legend effects: ↔, no significant change; ↑, significant increase; ↓, significant decrease; ^{X}, significant inhibition of stressor induced effect; $^{\emptyset}$, no significant inhibition of stressor effect against; Loc, protein localization; GenX, gene expression; ProtX, protein expression. If not differently specified between brackets, the measurement of TJs, mucins, mucus, and epithelial structure refer to the colonic region.

Legend time exposure: →, it indicates 'followed by'. For example, "0.5h (PP) → 6h (PP+S)" corresponds to a study design in which a 0.5h exposure to source of (poly)phenols was performed, followed by 6h co-exposure to source of (poly)phenols and stressor.

For animal models: information on number of animals per treatment group, age, body weight, and percentage (%) of males is provided between brackets.

Other simple phenolics common names: 3,4,5-trihydroxybenzoic acid (gallic acid), 1,3,5-trihydroxybenzene (phloroglucinol), 3,4-dihydroxybenzoic acid (protocatechuic acid), 3-hydroxy-4-methoxybenzoic acid (isovanillic acid), 4-hydroxy-3-methoxybenzoic acid (vanillic acid), 4-hydroxybenzene carboxylic acid (4-hydroxybenzoic acid, p-hydroxybenzoic acid), phloroglucinaldehyde (2,4,6-trihydroxybenzaldehyde), dihydrocaffeic acid (3-(3,4-dihydroxyphenyl)propanoic acid). Nomenclature based on Kay et al.[103].

*: Theobromine (100 µM) did not represent a challenge for the gut barrier integrity.

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