Table 1. Reported fatty acid compositions of oil from nuts of *P. sibirica* and *P. koraiensis*.

Source	Extraction method	Fatty acid analytical method	Fatty acid (% of total fatty acids)					Reference
			Palmitoleic	Stearic	Oleic	Linoleic	Pinolenic	
P. koraiensis	Chloroform-methanol	GC	4.2	1.8	25.5	48.4	14.9	Wolff & Bayard, 1995 [3]
P. koraiensis	Chloroform-methanol	GC	4.2	1.8	25.5	48.4	14.9	Asset *et al*., 1999 [22]
P. koraiensis	Hexane	GC	4.9	2.2	27.5	45.2	14.6	Destaillats *et al*., 2010 [2]
P. koraiensis	Supercritical-CO_2	GC-MS	5.8	2.9	28.5	41.8	15.6*	Chen *et al*., 2011 [18]
P. koraiensis	Chloroform-methanol	GC	5.3	2.1	25.7	46.0	13.7	Chung *et al*., 2017 [23]
P. koraiensis	Petroleum ether	GC	NR	2.2	26.2	44.8	14.2	Matthaus *et al*. 2018 [25]
P. sibirica	Acetone Reverse-phase	HPLC	6.3	2.5	23.8	49.0	17.0	Deineka & Deineka, 2003 [24]
P. sibirica	Cold-pressing	GC	4.8	2.8	24.7	46.0	19.2	Zadernowski *et al*., 2009 [20]
P. sibirica	Hexane	GC	4.4	2.5	25.5	43.5	18.3	Destaillats *et al*., 2010 [2]
P. sibirica	Petroleum ether	GC	NR	2.7	22.8	44.7	18.8	Matthaus *et al*. 2018 [25]

*reported as alpha linolenic acid in the paper

GC, gas chromatography; HPLC, high performance liquid chromatography; MS, mass spectrometry; NR, not reported

Table 2. Summary of studies investigating the effects of pine nut oil (PNO) or pinolenic acid (PLA) on appetite and weight gain

Model	PNO or PLA form	Details	Outcome investigated	Effect of PNO or PLA (% change where significant)	Reference
Male ICR mice	PNO extract (*P. koraiensis*)	Diet with 75 g/kg diet maize oil or PNO extract	Body weight Liver weight Feed intake Feed conversion efficiency	-37% -13% None -36%	Ferramosca *et al*., 2008 [36]
Double blind placebo controlled randomized crossover counter balanced design with 42 overweight women (BMI between 25 and 30 kg/m^2)	PNO extract (*P. koraiensis*) as NEFAs or TAGs in capsules	Six capsules with a total of 2, 4 or 6 g PNO TAGs or 2 g PNO NEFAs or olive oil (placebo) 30 min prior an *ad libitum* lunch	Food intake; 2, 4 or 6 g PNO TAGs Food intake; 2 g PNO NEFAs	None -9%	Hughes *et al*., 2008 [37]
Randomized, placebo controlled, double blind crossover trial with 18 overweight post-menopausal women (BMI between 25 and 30 kg/m^2)	PNO extract (*P. koraiensis*) as NEFAs or TAGs in capsules	Four capsules with 3 g PNO NEFAs, or PNO TAGs or olive oil with a light breakfast, over three test days, with a one-week washout period 4 hr post prandial responses	Hunger Fullness Desire to eat Prospective food consumption Plasma cholecystokinin-8 concentrations (PNO NEFAs, PNO TAGs) Plasma glucagon like peptide-1 concentrations (PNO NEFAs, PNO TAGs) Plasma ghrelin concentrations Plasma peptide YY concentrations	None None None None +60, +22% respectively +25%, none respectively None None	Pasman *et al*., 2008 [38]
Male C57BL/6 mice	PNO (*P. koraiensis*)	High fat diets for 12 weeks containing: 1) 10% kcal PNO or soybean oil + 35% kcal lard; 2) 20% kcal PNO or soybean	Body weight Weight gain	-10% across all PNO groups -17% across all PNO groups	Park *et al*., 2013 [39]

		oil + 25% kcal lard; 3) 30% kcal PNO or soybean oil + 15% kcal lard. Adipose tissue collected from epididymal, subcutaneous, and perirenal-retroperitoneal depots	Average daily food intake (PNO 10%, PNO 20%, PNO 30%) Average daily energy intake (PNO 10%, PNO 20%, PNO 30%) Adipose tissue weight (PNO 10%, PNO 20%, PNO 30%)	None, none -7% respectively None, none, -7% respectively -17%, none, -20%, respectively	
Male C57BL/6 mice	PNO (*P. koraiensis*)	High fat diets for 12 weeks containing 30% energy from PNO or soybean oil + 15% energy from lard Skeletal muscle tissue samples collected	Body weight Intramuscular lipid accumulation	-13% -40%	Le *et al*., 2012 [40]
Male C57BL mice	*PNO (P. koraiensis)*	High fat diets, fed *ad libitum* for 12 weeks, containing 10% energy from PNO or soybean oil + 35% energy from lard White adipose tissue collected from epididymal, abdominal subcutaneous, and retroperitoneal-perirenal depots	Body weight gain White adipose tissue Sirtuin 3 protein expression in white adipose tissue (epididymal fat pad)	-10% -18% +62.5%	Park *et al*., 2016 [41]
Male C57BL/6N mice	PNO (P. koraiensis)	High fat diets for 12 weeks containing 30% energy from PNO or soybean oil + 15% energy from lard White adipose tissue collected from epididymal, abdominal subcutaneous, and retroperitoneal-perirenal depots	Body weight Weight gain White adipose tissue	-9% -15% -20%	Zhu *et al*., 2016 [42]

BMI, body mass index; NEFA, non-esterifed fatty acid; TAG, triglyceride

Table 3. Summary of studies investigating the effects of pine nut oil (PNO) or pinolenic acid (PLA) on blood and hepatic lipids

Model	PNO or PLA form	Details	Outcome(s) investigated	Effect of PNO or PLA (% change where significant)	Reference
Male Sprague-Dawley rats	PNO *(P. koraiensis*)	Diet with 5 g/kg diet cholesterol and 100 g/kg diet PNO, safflower oil or flaxseed oil for 30 days	Plasma cholesterol Plasma TAGs Plasma PLs Hepatic cholesterol Hepatic TAGs Hepatic PLs	None None None None None None	Sugano *et al*., 1994 [32]
Male Wistar rats	PNO *(P. koraiensis or P. pinaster*)	Diet with 50 g/kg diet PNO (*P. koraiensis)* or a mixture of safflower, oleic-acid enriched sunflower and flaxseed oils (control) for 4 weeks Diet with 50 g/kg diet PNO (*P. pinaster)* or a mixture of safflower, oleic-acid enriched sunflower and flaxseed oils (control) for 4 weeks	Serum cholesterol Serum TAGs Serum PLs Serum VLDL cholesterol Serum VLDL TAGs Serum cholesterol Serum TAGs Serum PLs Serum VLDL cholesterol Serum VLDL TAGs	None None None None None None -30% None -33% -41%	Asset *et al*., 1999 [22]
HepG2 cells	Fatty acid extract of *P. koraiensis*	Incubation with 1 mM high-pinolenic acid containing FA extract for 2 h and then treated with Dil-LDL label (10–90 ug/mL) for 2 h at 4 and 37°C	Internalisation of labelled-LDL	+42%	Lee *et al*., 2004 [48]
Male ICR mice	PNO extract *(P. koraiensis*)	Diet with 75 g/kg diet maize oil or PNO extract for 8 weeks	Plasma cholesterol Plasma TAGs Plasma PLs Hepatic cholesterol Hepatic TAGs Hepatic PLs	-21% -32% -29% -10% -21% -10%	Ferramosca *et al*., 2008 [38]
Male and female Wistar rats	PNO *(P. koraiensis*)	Diet with 2.0, 4.0 or 8.0 g/kg diet per day PNO or high fat diet with 88 g/kg lard or control diet for 4 weeks	Serum cholesterol Serum TAGs	None None for 2 g/kg PNO; -32% for 4 g/kg PNO; none for 8 g/kg PNO	Chen *et al*., 2011 [18]

Male C57BL/6 mice	PNO (*P. koraiensis*)	Diet with 10% energy from PNO or soybean oil + 35% energy from lard for 12 weeks	Hepatic TAGs	-26%	Park *et al*., 2016 [41]
Male C57BL/6N mice	PNO (*P. koraiensis*)	Diet with 30% energy from PNO or soybean oil + 15% energy from lard for 12 weeks	Serum NEFAs Serum TAGs Hepatic TAGs	None None None	Zhu *et al*., 2016 [42]

LDL, low density lipoprotein; NEFA, non-esterified fatty acid; PL, phospholipid; TAG, triglycerides; VLDL, very low density lipoprotein

Table 4. Summary of study investigating the effect of pine nut oil (PNO) or pinolenic acid (PLA) on Insulin sensitivity

Model	PNO or PLA form	Details	Outcome investigated	Effect of PNO or PLA (% change where significant)	Reference
Male C57BL/6 mice	PLA or PNO (*P. sibirica*)	30 minutes prior to an oral glucose load (3 g/kg body weight) mice were given PNO (1 g/kg body weight), PLA (100 mg/kg body weight), or maize oil (1 g/kg body weight) by gavage.	Blood glucose concentration	-11% with PNO at 30 minutes after glucose challenge -26% with PLA at 30 and 60 minutes after glucose challenge	Christiansen *et al*. 2015 [52]

Table 5. Summary of studies investigating the effects of pine nut oil (PNO) or pinolenic acid (PLA) on inflammation

Model	PNO or PLA form	Details	Outcome(s) investigated	Effect of PNO or PLA (% change where significant)	Reference
Male Wistar rats	PNO *(P. sibirica)*	300 mg/kg bodyweight PNO for 2 days and 4 h prior to carrageenan injection into right hind paw and exposure of the paw to a temperature of 55°C	Inflammation (paw volume) 3, 12 and 24 hr after carrageenan injection Antipyretic effect (surface temperature of adjuvant-inflamed paw) 3, 12 and 24 hr after carrageenan injection Analgesic effect (response time to 55°C thermal-induced hot-plate) 3, 12 and 24 hr after	-24%, -36%, -45% respectively -5, -10, -10% respectively +118%, +120%, none	Shikov *et al*., 2008 [5]
Murine macrophages RAW264.7 cells	PLA	10, 25, 50 or 100 µM PLA for 24 hr followed by LPS stimulation (0.1 ug/mL) for 16 hr	Production of PGE_1 by RAW264.7 cells (10, 25, 50 and 100 µM PLA) Protein expression of COX-2 (50 µM PLA)	-33, -49, -73, -84% respectively None	Chuang *et al*., 2009 [6]
Human breast cancer MDA-MB-231 cells	PLA	50 or 100 µM PLA for 24 hr followed by TPA stimulation (0.1 ug/mL) for 12 hr 100 µM PLA for 24 hr followed by TPA stimulation (0.1 ug/mL) for 12 hr	Production of PGE_2 (50 and 100 µM PLA) Protein expression of COX-2 in MDA-MB-213 cells mRNA expression of COX-2 MDA-MB-213 cells	-50, -75% respectively -55% -55%	Chen *et al*., 2011 [29]
Murine macrophage RAW264.7 cells and rat primary peritoneal macrophages	PLA	25, 50 and 100 µM PLA for 24 hr followed by LPS stimulation (0.1 µg /mL) for 16 hr 50 and 100 µM PLA for 24 hr followed by LPS stimulation (0.1 µg /mL) for 8 hr 50 and 100 uM PLA for 24 hr followed by LPS stimulation (0.1 µg/mL) for 30 min	Production of PGE_2 by RAW264.7 cells (50 and 100 µM PLA) Production of PGE_2 by peritoneal cells (25 and 50 µM PLA) Protein expression of COX-2 in RAW264.7 cells (50 and 100 µM PLA) NFκB/p65 protein ratio in RAW264.7 cells (50 and 100 µM PLA) Phosphorylated-p38/p38 protein ratio in RAW264.7 cells (50 and 100 µM PLA)	-67, -80% respectively None, -13% respectively -20, -40% respectively -40, -50% respectively -25, -40% respectively	Huang *et al*., 2014 [7]

		50 and 100 µM PLA for 24 hr followed by LPS stimulation (0.1 µg/mL) for 15 min	Phosphorylated-JNK/JNK protein ratio in RAW264.7 cells (50 and 100 µM PLA) Phosphorylated-ERK/ERK protein ratio in RAW264.7 cells (50 and 100 µM PLA)	-25, -30% respectively -40, -30% respectively	
Murine microglial BV-2 cells and rat primary peritoneal macrophages	PLA	50 µM PLA for 24 hr followed by LPS stimulation (0.1 µg/mL) for 16 hr	Production of IL-6 by BV-2 cells Production of TNF-α by BV-2 cells Production of NO by BV-2 cells Production of PGE_2 by BV-2 cells Protein expression of iNOS in BV-2 cells Protein expression of COX-2 in BV-2 cells Production of NO by peritoneal cells Production of PGE_2 by peritoneal cells	-71% -27% -41% -89% -53% -10% -31% -35%	Chen *et al*., 2015 [8]
THP-1 macrophages	PLA	10, 25, 50 and 100 µM PLA for 24 hr followed by LPS stimulation (0.2 µg/mL) for 16 hr	Production of TNF-α (10, 25, 50 and 100 µM PLA) Production of IL-6 (10, 25, 50 and 100 µM PLA) Production of PGE_2 (10, 25, 50 and 100 µM PLA) Protein expression of COX-2 (50 and 100 µM PLA)	None, none, -9, -18% respectively -9, -24, -33, -48% respectively -55, -67, -78, -83% respectively -20, -25% respectively	Chen *et al*., 2019 [9]
Male ICR mice	PLA	Ears intradermally injected with PLA (3 µg) for 18 hr followed by TPA injection (5 µg) for 6 or 24 hr Topical application of PLA (3 µg) to dorsal skin followed by TPA injection (5 µg) for 2 hr	Ear swelling Ear thickness COX-2 protein expression in mouse ear tissue homogenates Infiltration of - leukocytes ($CD45^+$) - neutrophils ($Ly6G^+CD45^+$) - macrophages ($F4/80^+CD45^+$) Back skin cell free supernatant concentrations of - IL-1β - IL-6 - TNF-α - PGE_2 Back skin tissue homogenate protein expression of - Phosphorylated-p38	-29% -15% -53% -63% -50% -71% -79% -68% -42% -51% -55%	Chen *et al*., 2019 [9]

			- Phosphorylated -JNK - Phosphorylated -ERK	None None	
HepG2 cells	PLA	25 µM PLA for 12 hr PLA followed by oleic acid stimulation (0.5 mM)	Production of NO by HepG2 cells	-60%	Zhang *et al*., 2019 [10]
EA.hy296 cells	PLA	10, 25 and 50 µM PLA for 48 hr followed by TNF-α stimulation (1 ng/ mL) for 24 hr	Production of soluble ICAM-1 (10, 25, 50 µM PLA) Production of MCP-1 (10, 25, 50 µM PLA) Production of IL-6 (10, 25, 50 µM PLA) Production of IL-8 (10, 25, 50 µM PLA) Production of RANTES (10, 25, 50 µM PLA)	-15, -23, -24% respectively None, none, -25% respectively None None None, none, -46% respectively	Baker *et al*., 2020 [11]
		50 µM PLA for 48 hr followed by TNF-α stimulation (1 ng/ mL) for 1 hr	Phosphorylated NFκB/NFκB protein ratio	-50%	
		25 and 50 µM PLA for 48 hr followed by TNF-α stimulation (1 ng/ mL) for 6 hr	Cell surface expression of ICAM-1 Adhesion of THP-1 cells to EA.hy296 cell monolayers (25 and 50 uM PLA)	None None, -25%	

COX, cyclooxygenase; ERK, extracellular signal-regulated kinase; ICAM, intercellular adhesion molecule; IL, interleukin; iNOS, inducible nitric oxide synthase; JNK, c-Jun N-terminal kinase; LPS, lipopolysaccharide; MCP, monocyte chemoattractant protein; NFκB, nuclear factor kappa-light-chain-enhancer of activated B cells; NO, nitric oxide; PG, prostaglandin; RANTES, regulated on activation, normal T cell expressed and secreted; TNF, tumour necrosis factor; TPA, 12-O-tetradecanoylphorbol-13-acetate.

Table 6. Summary of studies investigating the effects of eicosatrienoic acid (ETA) on inflammation

Model	ETA form	Details	Outcome investigated	Effect of ETA (% change where significant)	Reference
Murine macrophage RAW264.7 cells and rat primary peritoneal macrophages	ETA	10, 25, 50 and 100 µM ETA for 24 hr followed by LPS stimulation (0.1 ug/mL) for 16 hr	Production of PGE_2 by RAW264.7 cells (10, 25, 50 and 100 µM ETA) Production of PGE_2 by peritoneal cells (25 and 50 µM ETA) Protein expression of COX-2 in RAW264.7 cells (50 and 100 µM ETA)	None, -47, -73, -80% respectively -40, -53% respectively None -40, -50% respectively	Huang *et al*., 2014 [7]
		50 and 100 µM ETA for 24 hr followed by LPS stimulation (0.1 ug/mL) for 30 min	Protein expression of NFκB/p65 ratio in RAW264.7 cells (50 and 100 µM ETA)		
		50 and 100 µM ETA for 24 hr followed by LPS stimulation (0.1 ug/mL) for 30 min	Phosphorylated-p38/p38 protein ratio in RAW264.7 cells (50 and 100 µM ETA) Phosphorylated-JNK/JNK protein ratio in RAW264.7 cells (50 and 100 µM ETA) Phosphorylated-ERK/ERK protein ratio in RAW264.7 cells (50 and 100 uM ETA)	-25, -30% respectively None, -20% respectively -20, -25% respectively	
Murine microglial BV-2 cells and rat primary peritoneal macrophages	ETA	50 µM ETA for 24 hr followed by LPS stimulation (0.1 g/mL) for 16 hr	Production of IL-6 by BV-2 cells Production of TNF-α by BV-2 cells Production of NO by BV-2 cells Production of PGE_2 by BV-2 cells Protein expression of iNOS in BV-2 cells Protein expression of COX-2 in BV-2 cells Production of NO by peritoneal cells Production of PGE_2 by peritoneal cells	-40% None -26% -92% -30% None -36% -54%	Chen *et al*., 2015 [8]
Male ICR mice	ETA	Ears intradermally injected with ETA (3 µg) for 18 hr followed by TPA injection (5 µg) for 6 or 24 hr	Ear swelling Ear thickness	-29% -15%	Chen *et al*., 2019 [9]

		Topical application of ETA (3 µg) to dorsal skin followed by TPA injection (5 µg) for 2 hr	COX-2 protein expression in mouse ear tissue homogenates Infiltration of - leukocytes ($CD45^+$) - neutrophils ($Ly6G^+CD45^+$) - macrophages ($F4/80^+CD45^+$) Back skin cell free supernatant concentrations of - IL-1β - IL-6 - TNF-α - PGE_2 Back skin tissue homogenates protein expression of - p-p38 - p-JNK - p-ERK	-59% -50% -67% -77% -55% -39% -48% -33% -81% -58% None	
EA.hy296 cells	ETA	5 and 10 µM ETA for 48 hr followed by TNF-α stimulation (1 ng/ mL) for 24 hr 10 uM ETA for 48 hr followed by TNF-α stimulation (1 ng/ mL) for 1 hr 5 and 10 µM ETA for 48 hr followed by TNF-α stimulation (1 ng/ mL) for 6 hr	Production of soluble ICAM-1 (5, 10 µM ETA) Production of MCP-1 (5, 10 µM ETA) Production of IL-6 (5, 10 µM ETA) Production of IL-8 (5, 10 µM ETA) Production of RANTES (5, 10 µM ETA) Protein expression ratio of phosphorylated NFκB/NFκB Cell surface expression of ICAM-1 Adhesion of THP-1 to EA.hy296 cell monolayers (5 and 10 µM ETA)	-21, 20% respectively -16, -22% respectively -29, -21% respectively None -70, -60% respectively -46% (p=0.06) None -55, -55% respectively	Baker *et al*., 2020 [11]

COX, cyclooxygenase; ERK, extracellular signal-regulated kinase; ICAM, intercellular adhesion molecule; IL, interleukin; iNOS, inducible nitric oxide synthase; JNK, c-Jun N-terminal kinase; LPS, lipopolysaccharide; MCP, monocyte chemoattractant protein; NFκB, nuclear factor kappa-light-chain-enhancer of activated B cells; NO, nitric oxide; PG, prostaglandin; RANTES, regulated on activation, normal T cell expressed and secreted; TNF, tumour necrosis factor; TPA, 12-O-tetradecanoylphorbol-13-acetate.

Table 7. Summary of studies investigating the effects of pine nut oil (PNO) on immune function

Model	PNO form	Details	Outcome(s) investigated	Effect of PNO (% change where significant)	Reference
Male Brown-Norway rats	PNO (*P. koraiensis)*	Diet with 100 g/kg diet of PNO or sunflower oil with immunisation on day 14 and 35 with 10 mg of intraperitoneal ovalbumin			Matsuo *et al*., 1996 [33]
		Spleen lymphocytes collected and cultured for 6 or 24 hrs	The proportion of $CD4^+$ T cells in spleen lymphocytes	+9%	
			The proportion of $CD8^+$ T cells in spleen lymphocytes	None	
			The $CD4^+/CD8^+$ T cell ratio in spleen lymphocytes	None	
			Production of IgG by spleen lymphocytes	+23%	
			Production of IgE by spleen lymphocytes	+43%	
		Rat peritoneal exudate cells collected from abdominal cavity	Production of LTB_4 by peritoneal exudate cells	+56%	
Male C57BL/6 mice	PNO (*P. koraiensis)*	High fat diets (45% energy from fat) for 12 weeks: 1) 10% kcal PNO or soybean oil + 35% kcal lard; 2) 20% kcal PNO or soybean oil + 25% kcal lard; 3) 30% kcal PNO or soybean oil + 15% kcal lard.	Splenocyte proliferative response to Con A and LPS	None	Park *et al*., 2013 [39]
		Cells collected from the spleen and stimulated with 0.5 or 1.5 mg/L Con A or 5, 15 or 30 mg/L LPS for 72 h	Production of IL-2 and IFN-y by splenocytes in response to Con A	None	
		Cells collected from the spleen and stimulated with 5 mg/L Con A for 48 h	Production of IL-6 by splenocytes in response to LPS	None	

		Cells collected from the spleen and stimulated with 10 mg/L LPS for 24 h	Production of IL-1β by splenocytes in response to LPS Production of PGE_2 by splenocytes in response to LPS	None for 10% PNO; none for 20% PNO; +54% for 30% PNO None	

ConA, concanavalin A; Ig, immunoglobulin; IL, interleukin; LPS, lipopolysaccharide; LT, leukotriene, PG, prostaglandin

Table 7. Comparison of the anti-inflammatory effect of four omega-3 fatty acids and pinolenic acid (PLA) in cultured EA.hy296 cells.
EA.hy296 cells were incubated with 50 μM fatty acid for 48 hours and were then stimulated with tumour necrosis factor-α (1 ng/ml). Nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB) activation (phosphorylation of the p65 subunit) was measured by Western blotting after 1 hour. Cyclooxygenase (COX)-2 protein was measured by Western blotting after 16 hours. Concentrations of interleukin (IL)-6, monocyte chemoattractant protein (MCP)-1 and regulated on activation, normal T cell expressed and secreted (RANTES) in the culture medium were measured by multiplex immunoassays after 24 hours. Data are summarised from Baker *et al*. [11, 67], apart from that marked * which is not published. Arrows indicate no effect (↔), an increase (↑) or a decrease (↓) compared with stimulus alone; the number of arrows used indicates the size of the effect.

	Effect of the fatty acid at 50 μM				
	Alpha-linolenic acid	Stearidonic acid	Eicosapentaenoic acid (EPA)	Docosahexaenoic acid (DHA)	PLA
IL-6 (pg/ml)	↔	↔	↓↓	↓↓	↔
MCP-1 (pg/ml)	↔	↓	↓↓	↓↓↓	↓
RANTES (pg/ml)	↔	↔	↓↓	↓↓↓	↓↓
NF-κB activation	↑	↔	↔	↓↓↓	↓
COX-2 protein expression	↔	↔	↓	↓↓	↓*