Table S1. Modulation of 5-LOX activity and comparison with COX-2 activity by (poly)phenols in cellular models. 1

Cellular model	Metabolite and assay conditions	Biological activity on 5-LOX and(or) COX-2 and molecular associated events	Effect on 5-LOX enzyme	Effect on COX-2 enzyme	References
Guinea pig isolated leukocytes	NDGA (0.5 – 30 μM)	↓LTB_4, 5-HETE and di-hydroxy acids formation (IC_{50} ~ 2 μM) in A23187-stimulated cells in a dose-dependent manner	Not evaluated	Not evaluated	[1]
Isolated peritoneal mouse macrophages (prelabelled with [^{14}C]-arachidonic acid) and rat neutrophils. Cell-fee assays with soybean 15-LOX were also carried out.	Quercetin and NDGA (0.01-100 μM).	Effects in A23187-stimulated rat neutrophils: ↓LTB_4 and 5-HETE formation in cells treated with quercetin (IC_{50} = 6.2 μM) and NDGA (IC_{50} = 1 μM); ↓PGE_2 and TxB_2 synthesis in cells treated with quercetin (IC_{50} = 6.2 and 18.0 μM, respectively) and NDGA (IC_{50} = 42.0 and 17.6 μM, respectively). Effects in zymosan-stimulated mouse macrophages: ↓PGE_2 and 6-Keto-$PGF_{1\alpha}$ formation in cells treated with quercetin (IC_{50} = 8.2 and 8.5 μM, respectively) and NDGA (IC_{50} = 2.4 and 4.2 μM, respectively). Quercetin and NDGA inhibited soybean 15-LOX activity (IC_{50} = 3.2 and 3.6 μM, respectively) in a cell-free assay.	Not evaluated.	Not evaluated.	[2]
Mouse mast tumor cells and rat-isolated platelets. Enzymatic assays with 5-LOX and	Caffeic acid and its phenethyl ester (CAPE) isolated from	↓LTC_4 and LTD_4 synthesis (only caffeic acid at 10 and 100 μM); ↓AA-	↓5-LOX activity by caffeic acid (IC_{50} = 3.7) and	↑COX-2 activity by caffeic acid	[3]

COX-2 obtained from cloned mastocytoma P-815,2-E-6 cells were also carried out.	*Artemisia rubripes* Nakai (0.1-100 μM).	induced platelet aggregation; ↓12-HETE formation (IC_{50} = 30 μM); no effect on HHT and TxB_2 formation at <10 μM, but at higher doses (100 μM) exerted an inhibitory effect (40% HHT and 80% 12-HETE); no effect on ADP-induced platelet aggregation.	CAPE (IC_{50} = 0.48 μM)	(64%) and CAPE (188%)	
Human and porcine leukocytes and platelets. COX activity was tested in microsomes from ram vesicular glands.	6,7,4'-trihydroxyisoflavan (1 μM – 1 mM).	↓5-HETE, 12-HETE, and LTB_4 formation, while sparing the production of HHT (15 μM) in activated (human and porcine) leukocytes; ↓12-HETE formation without inhibiting the synthesis of TxB_2 and HHT in platelets (at 100 μM); IC_{50} values for 12-LOX (human platelets) and 5-LOX (leukocytes) were 22.0 and 1.6 μM, respectively.	Not evaluated.	↓HHT, $PGF_{2\alpha}$, PGD_2, and PGE_2 synthesis in ram seminal vesicle microsomes (IC_{50} = 200.0 μM). Total inhibition at 1 mM.	[4]
Human isolated platelets and leukocytes	NDGA	↓5-HETE (IC_{50} = 0.2 – 0.3 μM), LTB_4 (IC_{50} = 0.5 μM), LTC_4 (IC_{50} = 0.2 – 0.5 μM), Δ^6-trans-LTB_4 (IC_{50} = 0.2 μM), ω-OH-LTB_4 (IC_{50} = 2 μM), 12-HETE (IC_{50} = 5 – 30 μM), 5*S*,12*S*-diHETE (IC_{50} = 0.2 μM), 15-HETE (IC_{50} = 30 μM) and HHT (IC_{50} = 5 – 100 μM)	Not evaluated	Not evaluated	[5]
Human isolated platelets and leukocytes	NDGA (0.1 – 100 μM)	↓5-HETE, LTB_4, LTC_4 and 12-HETE	Not evaluated	Not evaluated	[6]
Human-isolated PMNL from healthy donors	Caffeic acid (1 μM) and esculetin (10 μM)	↓5-HPETE and 5-HETE release in Streptolysin 0-stimulated PMNLs.	Not evaluated.	Not evaluated.	[7]

Leishmania donovani-infected macrophages	NDGA (3 μM)	↓5-HETE and 12- or 15-HETE in infected cells	Not evaluated	Not evaluated	[8]
Human isolated leukocytes	NDGA	↓5-HETE (IC_{50} = 0.6 μM) and weak effect on PGE_2 formation (IC_{50} = 119 μM) in A23187-stimulated cells	Not evaluated	Not evaluated	[9]
Human colonic mucosa	NDGA (10 μg/mL)	↓sulfidopeptide-LTs in A23187-stimulated human colonic mucosa; no significant effect on PGE_2 formation	Not evaluated	Not evaluated	[10]
Human isolated neutrophils	NDGA (10 μM)	↓LTB_4 and 5-HETE formation in A23187-stimulated neutrophils; no effect on HHT synthesis	Not evaluated	Not evaluated	[11]
Human isolated leukocytes.	Gingerdione, [6]-gingerol, and curcumin.	↓5-HETE release by [6]-gingerol (14% at 20 μM) as well as by shogaol, capsaicin, gingerdione and curcumin (IC_{50} = 23, 100, 15.0 and 8.0 μM, respectively); ↓PGE_2 release (IC_{50} = 67, 73, 18.0, 68.0 and 52.0 μM for shogaol, capsaicin, gingerdione, [6]-gingerol, and curcumin, respectively) in A23187-activated leukocytes.	Not evaluated.	Not evaluated.	[12]
Human isolated PMNL	3,5-, 4,5-, and 3,4-di-*O*-caffeoylquinic acid, caffeoylmalic acid, caffeoyltartaric acid, rosmarinic acid, caffeic acid, and chlorogenic acid (1 μM – 1 mM).	↓LTB_4 and 5-HETE formation in A23187-stimulated PMNLs (IC_{50} = 55.6 – 92.5 μM and 214 – 918 μM for all compounds, respectively); ↓15-HETE formation only in the presence of rosmarinic acid (IC_{50} = 455 μM); ↑PGE_2 in the presence of 3,4-di-*O*-caffeoylquinic acid, caffeic acid, and caffeoylmalic acid; ↓HHT in the presence of the compounds tested (IC_{50} = 80.0 – 90.2 μM); chlorogenic acid was inactive.	Not evaluated.	Not evaluated.	[13]

Elicited rat peritoneal leukocytes.	Hypolaetin-8-glucoside, hypolaetin, and 14 other flavonoids (1 μM – 1 mM).	↓LTB_4 and TxB_2 production in A23187-stimulated leukocytes by various flavonoids. Glycosides were less active than their aglycones (i.e., hypolaetin-8-glucoside/hypolaetin; gossypin/gossypetin; rutin/quercetin; naringin/naringenin), with the exception of naringin/naringenin. The flavonoids that stimulated DNA degradation also showed 5-LOX inhibitory activity, whereas those that lacked capacity to degrade DNA were related to COX inhibition.	Not evaluated.	Not evaluated.	[14,15]
Rabbit peritoneal PMNLs	Isoliquiritigenin (10 and 30 μM).	↓[^{14}C]5-HETE production in a concentration-dependent manner in A23187-stimulated PMNLs; no inhibitory effect on PLA_2 activity obtained from rabbit platelet sonicates; ↓[^{14}C]12-HETE formation in rabbit platelet sonicates.	Not evaluated.	Not evaluated.	[16]
Porcine leukocytes	Isoflavonoids such as isoflavans and isoflavones (0.5 – 200 μM)	↓5-LOX products (5-HETE, 5-HPETE, LTB_4 and stereoisomers of LTB_4); structure-activity investigation showed more effective inhibition in the presence of isoflavans	Not evaluated	Not evaluated	[17]
Rat peritoneal neutrophils and human platelets	Curcumin (1–50 μM).	↓LTB_4 synthesis in stimulated (calcium/A23187) rat peritoneal neutrophils (IC_{50} = 30 μM; NDGA = 0.5 μM). ↓COX-1 (IC_{50} = 2 μM) and 12-LOX activity (30 μM) in platelets.	Not evaluated.	Not evaluated.	[18]
Rat resident peritoneal macrophages.	Baicalein (1, 10 and 100 μM).	↓LTC_4 synthesis in A23187-stimulated macrophages (IC_{50} = 9.5 μM)	Not evaluated.	Not evaluated.	[19]

Murine resident peritoneal macrophages.	Genistein (1–100 μM).	↓PGE_2 production (IC_{50} = 20.0 μM) in response to zymosan, calcium ionophore A23187, and phorbol myristate acetate (PMA) stimulation; ↓LTC_4 production in response to zymosan and calcium ionophore A23187 (IC_{50} = 15.0 and 10.0 μM, respectively). These effects were not exerted via inhibition of PLA_2, COX or LOX enzymes.	Not evaluated.	Not evaluated.	[20]
Rat peritoneal leukocytes	Tanetin, fisetin, 3-hydroxy-flavone (1 – 100 μM)	↓LTB_4, TxB_2 and PGE_2 in A23187-stimulated cells in the presence of tanetin (IC_{50} = 11 and 6-11 μM for 5-LOX and COX-2, respectively), fisetin (IC_{50} = 11 and 50 μM for 5-LOX and COX-2, respectively) and 3-hydroxyflavone (IC_{50} = 80 and 6-8 μM for 5-LOX and COX-2, respectively)	Not evaluated	Not evaluated	[21]
Human isolated PMNL	RSV, piceid, 2,3,4′,5-tetrahydroxystilbene-2-*O*-D-glucoside, α-(3,4-dihydroxy-phenyl)-cinnamic acid, α-(3,4-dihydro-xy-phenyl)-3-hydroxycinnamic acid, α-(3,4-dihydro-xy-phenyl)-4-hydroxycinnamic acid, α-(3,4-dihydro-xy-phenyl)-3,4-dihydroxycinnamic acid, 3,3′,4-trihydroxystilbene	↓5-HETE, 5,12-diHETE, 15-HETE, HHT and PGE_2 in A23187-stimulated cells in the presence of RSV (IC_{50} = 8.9, 6.7, 275, 4.4, 9.6 μM, respectively) and 3,3′,4-trihydroxystilbene (IC_{50} = 5.9, 0.63, 6.77, 19, 49 μM, respectively). Piceid only affected 5-HETE (IC_{50} = 267 μM) and 5,12-diHETE (IC_{50} = 201 μM) biosynthesis; no effects observed in the presence of the rest of compounds ↓LTC_4 in A23187-stimulated cells in the presence of RSV (IC_{50} = 1.37 μM) and 3,3′,4-trihydroxystilbene (IC_{50} = 0.88 μM); ↓β-glucuronidase release	Not evaluated	Not evaluated	[22]

		and ↑cAMP concentration in the presence of RSV and 3,3′,4-trihydroxystilbene			
RBL-1 and RBL-2H3 cells	Honokiol	↓LTB_4 and LTC_4 formation in A23187-stimulated RBL-1 and IgE-treated RBL-2H3 cells; no effect on PLA_2, LTC_4 synthase and LTA_4 hydrolase activity	↓LTB_4 and LTC_4 in cell-free assays	Not evaluated	[23]
Isolated rat Kupffer cells and human phagocytic liver cells.	Silibinin (10, 25, 100 and 200 μM).	↓LTB_4 formation (IC_{50} = 15 μM) and no effect on PGE_2 formation in A23187-stimulated Kupffer cells. ↓Dose-dependent of O_2^- and NO production (IC_{50} = 80 μM). No effect on TNF-α formation. ↓LTB_4 formation in freshly isolated human phagocytic liver cells (10 and 25 μM).	Not evaluated.	Not evaluated.	[24]
Human platelets, white blood and endothelial cells.	Silibinin (1–25 μM to determine LOX products and 1–100 μM to determine COX products).	↓LTB_4 formation (IC_{50} = 15 μM) and Cys-LT formation (IC_{50} = 14.5 μM) in A23187-stimulated human granulocytes, but no effect on PGE_2 formation. ↓PGE_2 formation in LPS-activated human monocytes (IC_{50} = 45 μM). ↓TxB_2 and 6-keto-$PGF_{1\alpha}$ formation (IC_{50} = 69 and 52 μM, respectively), in human platelets and A23187-stimulated endothelial cells, respectively. ↓Hypochlorite production (IC_{50} = 7 μM), but not of O_2^- production in PMA-activated human granulocytes.	Not evaluated.	Not evaluated.	[25]

Rat platelets and rat PMNL	2-(3,4-Dihydroxyphenyl) ethanol (DPE), 2-(4-Hydroxyphenyl) ethanol, 2-(3,4-dihydroxyphenyl) acetic acid, caffeic acid, protocatechuic acid, *p*-coumaric acid, *o*-coumaric acid, vanillic acid, and syringic acid (0.1 μM – 1 mM)	↓LTB_4 production in A23187-stimulated PMNLs and 12-HETE production in intact platelets (IC_{50} of DPE = 26.0 and 50.0 μM, respectively). DPE showed the highest inhibitory (compared with the rest of the compounds) activity against 5- and 12-LOX, especially in intact cells.	↓5-HETE synthesis (IC_{50} of DPE = 13.0) (5-LOX isolated from PMNLs)	↓12-HETE synthesis (IC_{50} of DPE = 4.2 μM), and no effect on TxB_2 synthesis (COX-1 and 12-LOX isolated from platelets)	[26]
PMNL from healthy donors.	Hydroxytyrosol (0.1 μM – 1 mM).	↓LTB_4 production (IC_{50} = 1.2 μM) and its ω-oxidized metabolites (20-hydroxy and 20-carboxy-LTB_4) in A23187-stimulated PMNLs	Not evaluated.	Not evaluated.	[27]
RBL-1 cells	YPE-01 (derived from yakuchinones), yakuchinone B, dimethyl-yakuchinone B; NDGA was used a control of 5-LOX inhibition	↓LTB4 and LTC4 biosynthesis in A23187-treated RBL-1 cells in the presence of YPE-01 (IC_{50} = 0.035 and 0.046 μM, respectively), yakuchinone B (IC_{50} = 0.49 and 0.61 μM, respectively), dimethyl-yakuchinone B (IC_{50} = 1.14 and 2.11 μM, respectively) and NDGA (IC_{50} = 0.27 and 0.5 μM, respectively)	↓5-LOX activity by YPE-01 (IC_{50} = 0.28 μM), yakuchinone B (IC_{50} = 0.37 μM), dimethyl-yakuchinone B (IC_{50} = 0.22 μM) and NDGA (IC_{50} = 0.49 μM) in cell-free assay	↓COX-1 and COX-2 activity by yakuchinone B and dimethyl-yakuchinone B in cell-free assays	[28]
Human PMNL from healthy donors.	*trans*-RSV (0.44 – 440 μM).	↓LTB_4, 6-trans- and 12-trans-epi-LTB_4 production in A23187-stimulated PMNLs (IC_{50} = 48.2±7.0 μM); formation of 5-LOX-derived metabolites was virtually abolished at 220 μM.	Not evaluated.	Not evaluated.	[29]
Bovine PMNL	Hyperoside, rutoside, and chlorogenic acid (25 – 100 μM).	No effect on LTB_4 or 12(*S*)-HETE biosynthesis at concentrations ≤100 μM in A23187-stimulated PMNLs.	Not evaluated.	Not evaluated.	[30]

Human isolated PMNLs and rat basophilic leukemia cells RBL-1	Myr-3-glur and NDGA	↓LTB_4 formation in A23187-stimulated PMNLs treated with Myr-3-glur for 2 h (IC_{50} = 2.2 μM) or with NDGA for 5 min (IC_{50} = 0.5 μM); no effect of Myr-3-glur in cells incubated for 5 min. Myr-3-glur inhibited AA-induced platelet aggregation and ↓PGE_2, PGD_2, and PGI_2 biosynthesis ex vivo (to a similar extent as indomethacin) ↓COX-1 activity obtained from platelets (IC_{50} = 0.5 μM) and ram seminal vesicle (IC_{50} = 10 μM)	↓5-LOX activity in a crude enzyme preparation from RBL-1 (IC_{50} = 0.1 μM for Myr-3-glur and IC_{50} = 0.26 μM for NDGA)	↓COX-2 activity (IC_{50} = 0.26 μM) obtained from sheep placenta	[31]
Rat peritoneal leukocytes.	Gnaphalin, quercetin and galangin (20 – 160 μM).	Gnaphalin effects: ↓LTB_4 production in A23187-stimulated rat peritoneal leukocytes (IC_{50} = 81.8±12.9 μM; ↓TxB_2 production in rat peritoneal leukocytes stimulated with A23187 (IC_{50} = 39.9±3.9 μM), chemotactic peptide fMLP (IC_{50} = 12.0 μM) and AA (IC_{50} = 57.7±5.1 μM); no effect on the secretion of lysozyme, myeloperoxidase and β-glucuronidase pro-inflammatory enzymes from neutrophil secretory granules; no scavenging effect against hydrogen peroxide or hypochlorous acid. Quercetin effects: inhibition of LTB_4 (100%) and TxB_2 (55%) at 160 μM. Galangin effects: inhibition of LTB_4 (11%) and TxB_2 (84%) at 40 μM.	Not evaluated.	Not evaluated.	[32]
Rat peritoneal leukocytes.	Oleuropein, tyrosol, hydroxytyrosol, and	↓LTB_4 production in A23187-stimulated rat peritoneal leukocytes treated	Not evaluated.	Not evaluated.	[33]

	caffeic acid (40, 100 and 200 μM).	with hydroxytyrosol, oleuropein, caffeic acid, and tyrosol (IC_{50} = 15, 80, 200, and 500 μM, respectively); ↓ROS production in PMA-stimulated rat leukocytes; no substantial inhibition on TxB_2 exerted by the compounds tested			
Human isolated PMNLs	3-methylcatechol, 4-methylcatechol, 4-nitrocatechol, guaiacol, pyrogallol, propylgallate, 1,2,4-trihydroxybenzene, 1,3,5-trihydroxybenzene (1.8 nM – 1800 μM)	↓LTB_4 (IC_{50} = 5 – 900 μM) and PGE_2 (IC_{50} = 45 – 900 μM) synthesis in A23187-stimulated cells (at concentrations higher than 18 μM); 1,3,5-trihydroxybenzene exerted no inhibition on LTB_4 formation (IC_{50} >> 1800 μM)	Not evaluated	Not evaluated	[34]
Human erythroleukemia K562 cells.	RSV (30 μM).	↓LTB_4 and PGE_2 synthesis in H_2O_2-treated K562 cells; ↓purified 15-LOX (IC_{50} = 25.0±3.0 μM) activity.	↓purified 5-LOX (IC_{50} = 2.5±0.3 μM) activity.	↓PGH synthase (IC_{50} = 20.0±2.0 μM) activity	[35]
Rat isolated peritoneal leukocytes	6-hydroxy-kaempferol 3,6-dimethyl ether; 6-hydroxy-kaempferol 3,6,4′-trimethyl ether; quercetagenin 3,6,3′-trimethyl ether; 6-hydroxy-luteolin 6-methyl ether; 6-hydroxy-luteolin 6,3′-dimethyl ether	↓TxB_2 (IC_{50} = 22 – 182 μM) and LTB_4 (IC_{50} = 58 – 182 μM) biosynthesis in A23187-stimulated cells	Not evaluated	Not evaluated	[36]
RBL-2H3	Magnolol (0.1 – 20 μM)	↓LTB_4 and LTC_4 formation (at 10 and 20 μM); no effect on IgE-induced β-hexosaminidase release; ↓AA release at 10 μM; ↓[Ca^{+2}] release in IgE-treated cells	↓LTB_4 and LTC_4 (using AA or LTA_4 as substrates) formation at 10 and	Not evaluated	[37]

			25 μM in cell-free assays		
Monocytic leukemia cells MM6, human platelets and PMNLs isolated from healthy donors.	Hyperforin (0.1 – 100 μM).	↓LTB_4 and 15-HETE formation in A23187-stimulated PMNLs (IC_{50} = 1.0-2.0 and >10 μM, respectively); ↓HHT production in thrombin- or A23187- and exogenous AA-stimulated human platelets (IC_{50} = 0.3, 3.0 and 3.0 μM, respectively) as well as in platelet lysates (IC_{50} = 3 μM). Hyperforin could not interfere with COX-2 product formation (6-keto-$PGF_{1\alpha}$) in MM6 cells; and did not significantly inhibit 12-LOX or 15-LOX in intact platelets or leukocytes, respectively.	↓purified 5-LOX (IC_{50} = 90 nM) activity acting via uncompetitive mechanisms.	Not evaluated.	[38]
Rat peritoneal leukocytes	Erycristagallin (≤100 μM)	↓LTB_4 formation in A23187-stimulated leukocytes (IC_{50} = 23.4 μM) without cytotoxic effects; no effect on COX-1 from platelets at 100 μM	Not evaluated.	Not evaluated.	[39]
RAW264.7 macrophages and HT-29 human colon cancer cells.	Curcumin and THC (10, 20 and 50 μM).	↓LTB_4 and PGE_2 formation as well as AA release in LPS-stimulated RAW264.7 cells at 10 μM; ↓AA release in A23187-stimulated HT-29 cells at 10 μM; ↓$cPLA_2$ activity from microsomal fraction of HT-29 cells; ↓$cPLA_2$ level and $cPLA_2$ phosphorylation in LPS-treated RAW264.7 cells at 50 μM; ↓$PGF_{2\alpha}$, PGE_2, PGD_2, HHT, 15-HETE and 11-HETE in LPS-stimulated RAW264.7 cell lysates treated with 0THC at 50 μM; at the same concentration curcumin reduced the biosynthesis of PGD_2, 15-HETE and 11-	↓Human recombinant 5-LOX expression in LPS-treated RAW264.7 cells (IC_{50} = 0.7 and 3 μM for curcumin and THC, respectively).	↓COX-2 expression in LPS-treated RAW264.7 cells (curcumin at 20 μM), but increase COX-2 levels without LPS stimulation.	[40]

		HETE; higher inhibitory effect on the peroxidase activity of COX-1 than that of COX-2			
Rat peritoneal leukocytes.	Sigmoidin A and sigmoidin B (5 – 100 μM).	↓LTB_4 in calcium/A23187- stimulated rat peritoneal leukocytes treated with sigmoidin A (IC_{50} = 31 μM), sigmoidin B (44% inhibition at the same concentration); apigenin used as reference compound also showed inhibitory activity (IC_{50} = 14 μM). No inhibition of COX-1 activity; no reduction of 12-HHT synthesis at 100 μM of both compounds.	Not evaluated.	Not evaluated.	[41]
PMNLs from healthy donors.	Curcumin, eugenol, cinnamaldehyde and quercetin (1 – 150 μM).	↓5-HETE production in PMNLs (IC_{50} = 30.0, 26.0, 35.0 and 25.0 μM for curcumin, eugenol, cinnamaldehyde and quercetin, respectively); NDGA (IC_{50} = 28.0 μM).	Not evaluated.	Not evaluated.	[42]
Neutrophils isolated from rats	Magnolol (0.1 – 10 μM)	↓COX products formation, but low effect on 5-LOX products biosynthesis at 3 μM; Inhibition of COX and 5-LOX products production at 10 μM; ↓TxB_2 formation (IC_{50} = 0.5 μM); ↑LTB_4 biosynthesis at concentrations <3 μM, but inhibition at higher concentrations; Magnolol alone modified 5-LOX distribution in the cells, ↑AA release (PLA_2 activity), ↑cPLA_2 translocation and phosphorylation (effects dose-dependent) and had no effect on MAPK phosphorylation. These effects were absent in the presence of A23187.	↓COX-1 and COX-2 activity (IC_{50} = 26.0 ± 1.9 and 31.2 ± 2.8 μM, respectively) in cell-free assays	Weak inhibition of 5-LOX activity (IC_{50} ~ 90 μM) in cell-free assay	[43]

BMMC cells	Ginkgetin (1 – 50 μM).	↓LTC_4 in BMMC activated with KL (100 ng/ml) (IC_{50} = 0.33 μM); ↓PGD_2 in BMMC activated with KL (100 ng/ml), IL-10 (100 U/ml) and LPS (100 ng/ml) (IC_{50} = 0.75 μM); ↓degranulation reaction in a dose dependent manner (IC_{50} = 6.52 μM)	Not evaluated.	↓COX-2 protein level.	[44]
Rat peritoneal neutrophils and RAW 264.7 macrophages	5-*O*-demethylnobiletin (0.01 – 10 μM)	↓LTB_4 formation in rat neutrophils (IC_{50} = 0.35 μM)	↓5-LOX activity (cell lysate) by 57% at 0.25 μM	↓COX-2 expression RAW cells (5-20% inhibition)	[45]
Human monocyte line U937.	Procyanidin B_2 (50 and 100 μM).	↓LOX-1 protein and mRNA levels in ox-LDL treated macrophages.	↓5-LOX protein and mRNA levels in ox-LDL treated macrophages.	Not evaluated.	[46]
BMMC	Five coumarins (psoralen, xanthotoxin, scopoletin, umbelliferone, and (+)-marmesin) and three flavonoids (apigenin, luteolin and cynaroside) (12.5 and 25.0 μg/mL).	↓LTC_4 production in BMMC activated with KL (100 ng/ml) at 25.0 μg/mL; ↓PGD_2 formation in BMMC activated with KL (100 ng/ml), IL-10 (100 U/ml) and LPS (100 ng/ml) at 12.5 μg/mL. All compounds showed COX-2/5-LOX dual inhibitory activity.	Not evaluated.	Not evaluated.	[47]
BMMC cells	Methyl gallate (5 – 160 μM).	↓LTC_4 (IC_{50} = 5.3 μM) in BMMC activated with KL (100 ng/ml). ↓PGD_2 (IC_{50} = 17.0 μM) in BMMC activated with KL (100 ng/ml), IL-10 (100 U/ml) and LPS (100 ng/ml).	Not evaluated.	↓COX-2 activity (colorimetric COX inhibitor screening assay kit) (IC_{50} = 19.0 μM); no effect on COX-2 protein levels at ≤80 μM.	[48]
BMMC cells	Ochnaflavone (1.5 – 50 μM).	↓LTC_4 (IC_{50} = 6.5 μM) in BMMC activated with KL (100 ng/ml).	Not evaluated.	↓COX-2 protein levels.	[49]

		↓PGD_2 (IC_{50} = 0.6 μM) in BMMC activated with KL (100 ng/ml), IL-10 (100 U/ml) and LPS (100 ng/ml); ↓Degranulation reaction in a dose dependent manner (IC_{50} = 3.0 μM).			
PMNLs from healthy donors.	Eugenol (5 – 60 μM).	↓LTC_4 and 5-HETE in A23187- and AA-stimulated PMNLs (IC_{50} = 30.0 and 26.0 μM, respectively).	Not evaluated.	Not evaluated.	[50]
Human peripheral blood eosinophils	Genistein (1nM – 10 μM)	↓LTC_4 in A23187-stimulated cells (IC_{50} = 80 nM); ↓p38 and MK2 phosphorylation	↓5-LOX translocation	Not evaluated	[51]
Rat peritoneal leukocytes.	Sakuranetin, 7-*O*-methylaromadendrin and 3-acetyl-7-*O*-methylaromadendrin (5 – 100 μM).	↓LTB_4 production A23187-stimulated rat peritoneal leukocytes treated with 7-*O*-methylaromadendrin, sakuranetin, and 3-acetyl-7-*O*-methylaromadendrin (IC_{50} = 62, 9 and 15 μM, respectively); as a reference compound, apigenin also showed inhibitory effects (IC_{50} = 14 μM); ↓PLA_2 activity (only 7-*O*-methylaromadendrin); ↓Elastase release (only sakuranetin at 100 μM); none of the flavanones tested inhibited PGE_2 biosynthesis in RAW 264.7 mouse macrophages.	↓LTB_4 production in homogenized rat peritoneal polymorphonuclear leukocytes (only sakuratenin at 20 μM).	Not evaluated.	[52]
Human gastric epithelial cells (AGS) and murine macrophage RAW264.7	NDGA and geraniin (10 μM).	↓5-HETE production in AGS cells; ↓IL-8 and TNF-α in AGS cells and macrophages; attenuation of $cPLA_2$ induction by NDGA, but not geraniin.	↓5-LOX protein levels.	No effect on COX-2 protein levels.	[53]
BMMC cells	Meso-dihydroguaiaretic acid (0.8 – 25 μM).	↓LTC_4 (IC_{50} = 1.3 μM) in BMMC activated with KL (100 ng/ml); ↓PGD_2 (IC_{50} = 9.8 μM) in BMMC activated with KL (100 ng/ml), IL-10 (100 U/ml) and LPS (100 ng/ml); ↓Degranulation	Not evaluated.	No effect on COX-2 protein levels.	[54]

		reaction in a dose dependent manner (IC_{50} = 11.4 μM).			
PMNLs from healthy donors.	Carnosic acid and carnosol (0.03 – 30 μM).	↓LTB_4, 5(*S*),12(*S*)-diHETE, and 5-H(p)ETE in A23187-stimulated PMNL treated with carnosol and carnosic acid (IC_{50} = 7.0 and 15-20 μM, respectively); ↓12-HETE and 12-HPETE synthesis in A23187-stimulated PMNL treated with carnosol (IC_{50} = 13 μM), but no effect on cells treated with carnosic acid; Antagonise intracellular Ca^{2+} mobilisation induced by a chemotactic stimulus, and attenuate formation of ROS and the secretion of human leukocyte elastase.	↓5-LOX activity (IC_{50} = 0.1 and 1.0 μM for carnosic acid and carnosol, respectively)	Not evaluated.	[55]
PBMC isolated from whole human blood.	Quercetin, 3′-*O*-methylquercetin (MQ), quercetin-3′-*O*-sulfate (QS), quercetin-3-*O*-glucuronide (QG) and 3′-*O*-methylquercetin-3-*O*-glucuronide (MQG) (1 – 10 μM).	↓LTB_4 synthesis in A23187-stimulated PBMCs treated with quercetin (IC_{50} = 2.0 μM) and MQ at 2.0 μM; ↓PGE_2 formation in LPS-activated PBMCs treated with quercetin and MQ (IC_{50} = 2.0 μM); lack of effect for the rest of compounds tested	Not evaluated.	Not evaluated.	[56]
Rat adherent macrophages from granuloma	NDGA (10 μM)	↓LTB_4 synthesis in stimulated cells	↓5-LOX expression (mRNA and protein)	Not evaluated	[57,58]
BBMCs isolated from mice	Isolated phenolic compounds from *Ailanthus altissima* leaves	Scopoletin, quercetin and luteolin inhibited the biosynthesis of PGD_2 (IC_{50} = 39.2, 7.3 and 2.5 μM, respectively) and LTC_4 (IC_{50} = 59.9, 5.1 and 1.8 μM, respectively); no effect of astragalin and scopoline at the concentrations tested.	Not evaluated	Not evaluated	[59]

		The methanolic extract and solvent fractions of *Ailanthus altissima* inhibited PGD_2 (49.0 – 57.4%) and LTC_4 (96.7 – 99.8%) at 50 μg/mL			
Human neutrophils	Hyperforin (0.3 – 30 μM)	↓5-LOX product biosynthesis (IC_{50} = 1.9 μM) in intact neutrophils via inhibition of 5-LOX translocation to the nuclear membrane. This effect was reduced in the presence of OAG (IC_{50} ≥ 10 μM)	↓5-LOX activity in cell homogenates (IC_{50} ~ 30 μM), in partially purified (IC_{50} ~ 7 μM) and purified enzyme (IC_{50} = 1.6 μM). This inhibition occurs via interaction with the Trp residues within the 5-LOX C2-like domain and blocking the binding of 5-LOX with CLP. Besides, this inhibitory effect was independent of the redox tone and blocked in the presence of OAG (IC_{50} ≥ 10 μM) and PC.	Not evaluated	[60]
RBL-1 cells and RAW 264.7 cells.	(-)-Nyasol (2 – 100 μM).	↓Cys-LT production in A23187-treated RBL-1 cells at 2 – 10 μM. As a reference compound, NDGA also exerted inhibitory effects at 5 μM;	Not evaluated.	No effect on COX-2 protein levels.	[61]

		↓PGD_2 and NO production in LPS-treated RAW 264.7 cells at 1 – 100 μM.			
RBL-1 and RAW 264.7 cells	*Schisandra fructus* methanolic extract and the individual compounds such as vanillic acid; NDGA as control of 5-LOX inhibition	↓5-LOX products formation (Cys-LTs) y RBL-1 cells treated with the extract (IC_{50} = 71.1 μg/mL) and NDGA (IC_{50} = 0.2 – 1 μM); vanillic acid had no effect; the extract and vanillic acid exerted less than 50% inhibition against PGE_2 and NO formation at the concentrations tested.	Not evaluated	Not evaluated	[62]
Rat endothelial cells (YPEN-1).	Morin (1 and 5 μM).	↓ROS generation; ↓NF-κB activation (via reduced DNA binding activity, IκB*α* phosphorylation and p65/p50 nuclear translocation); modulation of ERK and p38 signal transduction; ↓iNOS protein levels in *t*-BHP-induced YPEN-1 cells.	↓5-LOX protein levels in *t*-BHP-induced YPEN-1 cells.	↓COX-2 protein levels in *t*-BHP-induced YPEN-1 cells.	[63]
Murine macrophage RAW264.7 cells.	Curcumin (0.63 – 80 μM).	↓PGE_2 formation in LPS-stimulated RAW264.7 cells; ↑HO-1 mRNA expression and protein level; no effect on iNOS (mRNA expression and protein level), $cPLA_2$ (mRNA expression)	No effect on 5-LOX mRNA expression.	No effect on COX-2 mRNA expression and protein level.	[64]
BMCMC cells	NDGA (3 μM).	↑PGE_2 and ↓LTB_4/LTC_4 production in BMCMCs stimulated with ConA (mimics IgE cross-linking), substance P (following culture of cells with IL-4) or A23187; ↓degranulation of BMCMCs stimulated with ConA and A23187.	Not evaluated.	Not evaluated.	[65]
RBL-1	13 phenolic compounds isolated from *Lonicera japonica* (20	The compounds that exerted the highest inhibition on 5-LOX products (Cys-LTs) formation were protocatechuic acid (35.8%), 3,5-	Not evaluated	Not evaluated	[66]

	μM); NDGA as control of 5-LOX inhibition	dicaffeoylquinic acid methylester (15.1%), luteolin (97.0%), quercetin 3-O-β-D-glucopyranoside (11.1%) and NDGA (100%)			
Human isolated PBMC	Quercetin (25 μM)	↓TLR-2 and TLR-4 mRNA expression; ↓NF-κB activation; ↓IL-6 biosynthesis; ↓iNOS mRNA expression; ↓PGE_2 biosynthesis	↓5-LOX production;	↓COX-2 mRNA expression; ↓COX production;	[67]
RBL-1 cells	Scopoletin, scopolin, scoparone, esculetin chlorogenic acid, quercetin, isorhamnetin-3-*O*-galactoside, isorhamnetin-3-*O*-robinobioside, capillarisin, and NDGA (0.1 – 50 μM)	↓LTB_4 biosynthesis in A23187-stimulated cells. The most effective compounds were NDGA (95.7% inhibition at 1 μM), as well as esculetin, quercetin, and capillarisin (IC_{50} = 6.6, 0.7 and 17.7 μM, respectively).	Not evaluated	Not evaluated	[68]
Rat peritoneal macrophages	*Platycladus orientalis* chloroform extract (12.5 – 100 μg/mL) and the individual compounds hinokiol and acacetin (12.5 – 100 μM); 12.5 μM NDGA was used as control of 5-LOX inhibition	↓5-HETE and LTB_4; ↓12-HHT; the extract showed no inhibitory effect on LTA_4 hydrolase	↓5-LOX activity (43.2% for honokiol and 48.8% for acacetin at 100 μM; IC_{50} = 7.1 μM for NDGA) in a cell-free assay	Moderate or weak COX-2 inhibition in cell-free assays	[69]
RBL-2H3 cells	Extracts of *Foeniculum vulgare* (12.5 – 200 mg/mL), its individual compounds (50 μM) and 1 μM NDGA as positive control	↓5-LOX products (Cys-LTs) formation in cells treated with the extracts (only at 200 μg/mL); the individual phenolics (scopoletin and umbelliferone) had no effect on 5-LOX activity; 1μM NDGA exerted a strong inhibition (92.4%)	Not evaluated	Not evaluated	[70]

RBL-2H3 cells	Macelignan (5, 10 and 20 μM)	No cytotoxic effect; ↓β-hexosaminidase (8 – 32% inhibition) and histamine release (8 – 27% inhibition); ↓Ca^{+2} intracellular concentration; ↓PGE_2 and LTC_4 biosynthesis; ↓IL-4, IL-13, and TNF-α formation; ↓Akt and MAPK phosphorylation	↓5-LOX mRNA expression	↓COX-2 mRNA expression	[71]
PMNL from healthy donors, whole human blood and HEK293 cells	Caffeic acid and CAPE (0.1-30 μM).	CAPE exerted a ↓LT biosynthesis (LTB_4, 20-COOH- and 20-OH-LTB_4 as well as 5-HETE) in thapsigargin-stimulated PMNLs (53-85% inhibition at 1 μM; IC_{50} = 0.52 μM) as well as in zymosan-stimulated whole blood treated (32% reduction at 1 μM; IC_{50} = 1.79 μM); CAPE also exerted a ↓AA release in thapsigargin-stimulated PMNLs (32% reduction at 1 μM); Caffeic acid exerted no effects.	CAPE exerted ↓5-LOX activity (IC_{50} = 0.13 μM) whereas caffeic acid had no effect on the enzyme isolated from 5-LOX-transfected HEK293	Not evaluated.	[72]
Rat basophilic leukemia (RBL-2H3) cells.	Panduratin A (1 – 20 μM).	The effects observed in A23187- and PMA-stimulated RBL-2H3 cells were: ↓LTB_4 and PGE_2 formation as well as ↓AA release; ↓Ca^{2+} influx and β-hexosaminidase and histamine secretion at 20 μM; ↓IL-4, IL-13, and TNF-α mRNA expression; ↓Akt, ERK, p38, and JNK phosphorylation	↓5-LOX mRNA expression.	↓COX-2 mRNA expression.	[73]
Primary avian polymorphonuclear leukocytes.	Caffeic acid (5 μM).	↓LTB_4 production in leukocytes stimulated with TLR agonists (FLG, PAM or CpG).	Not evaluated.	Not evaluated.	[74]
Feline esophageal epithelial cells.	Eupatilin (25-200 μM).	↓H_2O_2-induced cytotoxicity (dose-dependent effect), ↓p38 and JNK activation, and LTB_4 production at 150 μM (12 h pretreatment).	↓5-LOX expression in H_2O_2-induced cells at 150 μM (12 h pre-treatment)	Not evaluated.	[75]

Human neutrophils isolated from peripheral blood of healthy donors.	3,3′,4′-Tri-hydroxy-flavone, 3,5,7-tri-hydroxy-flavone, 3,7,3′-tri-hydroxy-flavone and 3,7,4′-tri-hydroxy-flavone (10 and 25 μM), NDGA and quercetin (10 μM)	↓LTB_4 production in A23187- and AA-stimulated neutrophils (except for 3,7,3′-tri-hydroxy-flavone at 10 μM); ↓oxidation of luminol, amplex red and APF by reactive species generated by PMA-stimulated neutrophils; ↓COX-1 activity in a cell-free system for 3,5,7-tri-hydroxy-flavone and 3,7,3′-tri-hydroxy-flavone in a concentration-dependent manner.	Not evaluated.	↓COX-2 activity in a cell-free system for 3,5,7-tri-hydroxyflavone in a concentration-dependent manner.	[76]
RAW264.7 cells and rat peritoneal macrophages.	Baicalein and its glycoside, baicalin (1.5 – 100 μM).	↓LTB_4 production in rat peritoneal macrophages in the presence of exogenous AA (IC_{50} = 35.6 μM); ↓PGE_2 in LPS-stimulated RAW264.7 cells by baicalein (IC_{50} = 28.6 μM).	No effect on 5-LOX expression (mRNA and protein level).	↓COX-2 mRNA expression and protein level in LPS-stimulated RAW264.7 cells.	[77]
Human isolated PMNL or monocytes	Cannflavin A and B (0.1 – 10 μM)	↓5-LOX products (LTB_4, tr-LTB_4, 5-HPETE) with IC_{50} = 1.6 – 2.4 μM for cannaflavin A; ↓PGE_2 biosynthesis (IC_{50} = 8.8 μM for cannaflavin A) in LPS stimulated monocytes; ↓12-HHT in platelets (IC_{50} > 10 μM for cannaflavin A)	↓5-LOX (IC_{50} = 0.8 and 0.9 μM for cannaflavin A and B, respectively) activity	↓mPGES-1 activity by both compounds (cannaflavin A showed IC_{50} = 1.8 μM); ↓COX-1 and COX-2 activity (cannaflavin A showed IC_{50} > 10 μM)	[78]
Human isolated neutrophils	Luteolin, NDGA, quercetin, 3′,4′-dihydroxyflavone, apigenin, acacetin, chrysoeriol, diosmetin, taxifolin, chrysin, (±)-eriodictyol (±)-naringenin and other related flavonoids (10 and 40 μM)	The highest inhibition of LTB_4 synthesis was exerted by luteolin (IC_{50} = 1.6 ± 0.3 μM), 3′,4′-dihydroxyflavone (IC_{50} = 1.7 ± 0.1 μM), quercetin (IC_{50} = 4.0 ± 1.2 μM), NDGA (56.5 ± 2.5% inhibition at 1μM) and eriodyctiol (53.4 ± 4.8% inhibition at 40 μM).	Not evaluated	Not evaluated	[79]

BMMC	Homoisoflavanone (5,7-di-hydroxy-3-(3-hydroxy-4-methoxy-benzyl)-chroman-4-one) (1.4 – 14.4 μM).	↓LTB_4, LTC_4 and PGD_2 in DNP-IgE and DNP-HSA-activated BMMCs; ↓mRNA level and release of IL-6 and TNF-α; ↓degranulation of BMCMCs; no effect on COX-1 protein levels	↓5-LOX protein levels in DNP-IgE and DNP-HSA-activated BMMCs.	↓COX-2 protein levels in DNP-IgE and DNP-HSA-activated BMMCs.	[80]
BMMCs-isolated from bone marrow of C57BL/6	Curcumin (1 – 10 μM)	↓LTC_4 and Ca^{+2} influx in IgE/Ag-induced BMMCs; ↓COX-2-dependent PGD_2 synthesis; ↓$cPLA_2$ phosphorylation and translocation; inhibition of NF-κB, MAPK, and Syk pathways (all the effects were dose-dependent).	↓5-LOX translocation	Not evaluated	[81]
PMNL from healthy donors.	Pinostilbene, rhapontigenin, isorhapontigenin, RSV, oxyresveratrol, pterostilbene	↓LTB_4 (IC_{50} = 18.5 ± 7.8 and 9.32 ± 3.3 μM for oxyresveratrol and pterostilbene, respectively; IC_{50} > 50 μM for the rest of compounds) Pinostilbene exerted the highest COX-1 and COX-2 inhibition (IC_{50} = 1.9 ± 1.6 and 0.35 ± 0.23, respectively), whereas rhapontigenin was the weakest compound (IC_{50} = 24.55 ± 10.38 and 36.12 ± 10.43, respectively)	Molecular docking analysis showed that pterostilbene formed hydrogen bonds with His372 and Thr364	Molecular docking analysis showed that pinostilbene formed hydrogen bonds with Arg129, Phe518 and Gln192;	[82]
PMNL from healthy donors.	Xanthohumol, xanthohumol C, 8-prenylnaringenin, 4-hydroxy-colupulone, humulone, cascadone and humudifucol (up to 10 μM).	↓LTB_4 and 5-HPETE in A23187- and AA-stimulated PMNLs treated with xanthohumol (IC_{50} = 2.9 μM); no effects observed with the rest of compounds.	Not evaluated.	Not evaluated.	[83]
Human peripheral neutrophils from human whole blood.	Daidzein, dihydrodaidzein, and equol (0.01 – 1 μM).	↓LTB_4 A23187- and AA- stimulated neutrophils (IC_{50} = 0.2 μM for equol; 20% of inhibition for daidzein and dihydrodaidzein 1 μM); no effect on the enzymatic hydrolysis of LTA_4 to LTB_4; ↓free radical peroxidation of AA (IC_{50}	Not evaluated.	Not evaluated.	[84]

		= 0.6 μM for daidzein and >1.0 μM for equol and dihydrodaidzein); ↓MPO activity (IC_{50} = 0.45, 0.7 and >1.0 μM for equol, dihydrodaidzein and daidzein, respectively)			
Isolated human PMNL	CAPE (1 μM)	↓5-LOX products	Molecular docking analysis showed affinity = -8.5 Kcal/mol and interaction with His372	Not evaluated.	[85]
RAW 264.7 macrophages	Isoorientin (1 – 25 μM; 16 h)	↓TNF-α, IL-1β, iNOS expression and NF-κB pathway;	↓5-LOX protein expression	↓COX-2 protein expression	[86]
Mouse mast cell line (PB-3c).	Daidzein, genistein and their glycosides (daidzin and genistin), equol, quercetin and kaempferol (50 μM; 48 h).	↓LTB_4 production A23187- and AA-stimulated PB-3c cells (100% inhibition exerted by equol, quercetin and kaempferol, 72.5% by genistein, and a weak but significant suppression by daidzin and daidzein).	Not evaluated.	Not evaluated.	[87]
Isolated human PMNL and platelets	Baicalein, apigenin, quercetin, CAPE, myricetin (0.1 – 20 μM)	↓5-LOX products (including LTB_4, 6-*trans*-LTB_4, 6-*trans*-12-*epi*-LTB_4, 20-OH-LTB_4, 20-COOH-LTB_4, and 5-HETE); IC_{50} = 11.0 and 5.97 μM in PMNL for baicalein and quecetin, respectively). ↓12-HETE (IC_{50} = 1.78, 1.34 and 1.28 μM, respectively) and 12-HHT (IC_{50} = 9.92, 2.91 and 3.79 μM, respectively) in platelets treated with baicalein, quercetin and CAPE	Molecular docking analysis using soybean 15-LOX; (i) CAPE´s affinity = -5.4 kcal/mol and interaction with Arg426, Ser510, His518 and Phe576 (ii) Baicalein´s affinity = -1.4 kcal/mol and interaction with	Not evaluated.	[88]

			Fe, His518 and Phe576 (iii) Quercetin´s affinity = 0.8 kcal/mol and interaction with Asp766, His518 and Phe576		
Isolated human PMNL and whole blood	CAPE (0.1 – 10 μM)	↓5-LOX products (including LTB_4, tr-LTB_4, 20-OH-LTB_4, 20-COOH-LTB_4, and 5-HETE); IC_{50} = 0.97 and 3.58 μM in PMNL and whole blood, respectively)	Molecular docking analysis into the active site of 5-LOX (cristal structure) showed affinity = -8.8 Kcal/mol and interaction with Leu420 and His372	Not evaluated	[89]
Caco-2	Hydroxytyrosol (1 μM)	↓PGE_2, LTB_4, 5-HETE, 12-HETE, 15-HETE, 13-HODE	Not evaluated.	Not evaluated.	[90]
RAW 264.7 macrophages	Ellagic acid-3,3′,4-trimethoxy-4′-*O*-α-L-rhamnopyranoside (1 – 100 μM for toxicity assays; 1 – 5 μM for anti-inflammatory assays)	↓NO, TNF-α, IL-6 and NF-κB expression; ↑IL-10	↓5-LOX level in culture medium	↓COX-2 level in culture medium	[91]
Human monocytes, neutrophils and platelets.	Ginkgolic acid (0.1 – 10 μM).	↓Tr-LTB_4 isomers and 5-HPETE in A23187-stimulated intact human neutrophils in the presence or absence of exogenous AA (IC_{50} = 3.8 and 2.9 μM, respectively); ↓12-HHT formation by isolated COX-1 (IC_{50} = 8.1 μM); ↓12-HHT and TxB_2 formation in AA-stimulated platelets (IC_{50} = 2.1 and 2.2 μM,	↓Tr-LTB_4 isomers and 5-HPETE synthesized by human recombinant 5-LOX (IC_{50} = 0.2 μM)	No effect on COX-2 activity (human recombinant isolated enzyme)	[92]

		respectively); ↓PGE_2, PGD_2, TxB_2, $PGF_{2\alpha}$, 11-HETE, 12-HHT, PGE_1 and TxB_1 in LPS-stimulated monocytes.			
PBMCs from healthy donors.	Apigenin, EGCG, genistein, naringenin, nobiletin, wogonin), RSV and its dimer (ε-viniferin), tetramer (hopeaphenol), and imine analogues (IRA) (1 – 10 μM)	↓LTB_4 production by A23187- stimulated neutrophils treated with genistein, resveratrol, IRA (1 and 10 μM) and ε-viniferin (10 μM); LC-MS based targeted oxylipin metabolomics showed that: RSV inhibited the COX-1/2 pathway and exerted a weak attenuation of the 12/15-LOX activity; ε-viniferin caused a clear substrate shunt towards the remaining AA cascade enzymes (15-LOX, COX-1/2, cytochrome P450); IRA had no impact on 15-LOX activity, but elevated the formation of COX-derived PGs, having no inhibitory effects on COX-1/2 activity.	Not evaluated.	Not evaluated.	[93]
Murine mast cell line (MC/9).	Kuwanon G and Morusin (0.5–10 μM).	↓LTB_4 production in PMA- and A23187-stimulated MC/9 mast cells treated with morusin (2 and 4 μM); ↓histamine production by kuwanon G (2.5–10 μM) and morusin (4 μM).	↓5-LOX nuclear protein level, but not cytoplasmatic level in PMA- and A23187- stimulated MC/9 mast cells treated with kuwanon G (2.5 – 10 μM) and morusin (4 μM)	Not evaluated.	[94]
BMMC	Taxifolin (dihydroquercetin) (1, 2 and 5 μM).	↓LTC_4 in IgE/Ag-stimulated and DNP-HSA-activated BMMCs.	↓5-LOX nuclear protein levels in	↓COX-2 protein levels in IgE/Ag-stimulated and	[95]

		↓IL-6 and MAPKs protein levels, translocation of $cPLA_2$ and Akt/IKK/NF-κB pathway in IgE/Ag-stimulated and DNP-HSA-activated BMMCs. ↓degranulation, histamine release, phosphorylation of PLCγ, and Ca^{2+} mobilization in IgE/Ag-stimulated and DNP-HSA-activated BMMCs.	IgE/Ag-stimulated and DNP-HSA-activated BMMCs.	DNP-HSA-activated BMMCs.	
PMNLs from healthy donors.	Uro-A, Uro-B, Uro-C and IsoUro-A, and their conjugates Uro-A glur, Uro-B glur, IsoUro-A-glur and Uro-A sulfate (1, 5 and 15 μM).	↓LTB_4 and 5-HETE (dose-dependent) synthesis in A23187/LPS-stimulated PMNLs treated with Uro-C (15 μM); ↓PGE_2 formation A23187/LPS- stimulated PMNLs treated with Uro-A or IsoUro-A (15 μM); ↓HKE_2 and HKD_2 production (5-LOX/COX-2 pathway) in A23187/LPS-stimulated PMNLs treated with Uro-A, IsoUro-A, and Uro-C at 15 μM; ↓HKD_2 in the cells treated with Uro-B at 15 μM.	↑No effect on 5-LOX protein level in A23187/LPS-stimulated PMNLs treated with Uro-C at 15 μM.	↓COX-2 protein level in A23187/LPS-stimulated PMNLs treated with Uro-A and IsoUro-A at 15 μM; no effect of these compounds on COX-2 activity	[96]
Caco-2	5,7 di-hydroxy-3,3′,4′-trimethoxyflavone and 3,5,6,7,4′-pentamethoxy-flavone	↓TNF-α and IL-1β as well as NF-κB activation compared to LPS-treated cells.	No effect on 5-LOX expression	↓COX-2 expression in LPS-treated cells	[97]
Human neutrophils	NDGA (1 μM)	↓TLB_4, tr-LTB_4, 20-OH-LTB_4, 5-HETE, 12-HETE and 15-HETE	No effect on 5-LOX expression	No effect on COX-2 expression	[98]
RAW 264.7 macrophages	Celery ethanol extract, and karafsin (apigenin-7-O-β-(5′-E-p-coumaroyl)-β-apiofuranoside)	No cytotoxic effects; ↓NO release (0.0625 – 1 mg/mL).	↓5-LOX activity (25 – 500 mg/mL)	↓COX-2 activity (25 – 500 mg/mL)	[99]

Rat basophilic leukemia cell line (RBL-2H3) cells.	Tricin (30.2 μM – 1.5 mM).	↓LTB_4, LTC_4 and PGE_2 formation in anti-DNP-IgE plus DNP-HAS-stimulated RBL-2H3 cells; ↓hexosaminidase release; ↓IL-4 and TNF-α level; ↓cPLA2, Akt, ERK, p38, JNK, protein kinase C, phospholipase C1, Lyn and Syk phosphorylation; minimal effect on Fyn.	↓5-LOX protein levels in anti-DNP-IgE plus DNP-HAS-stimulated RBL-2H3 cells.	↓COX-2 protein levels in anti-DNP-IgE plus DNP-HAS-stimulated RBL-2H3 cells.	[100]
Rat basophilic leukemia RBL-2H3 cells and human non–small-cell lung carcinoma A549 cells.	Red-kerneled rice proanthocyanidin -RRP- (catechin octamer) and catechin monomer (1 – 10 μM).	↓LTB_4 and PGE_2 formation in A23187-stimulated RBL-2H3 and A549 cells treated with RRP at 1 μM; RRP exerted inhibition of 12-LOX (IC_{50} = 39.0 μM) and p12-LOX (IC_{50} = 47.5 μM) activity; weak inhibitory effect on 15-LOX-2 (IC_{50} >100 μM); catechin exerted ↓15-LOX-2 (IC_{50} = 20.4 μM) and COX-1 (IC_{50} = 30 μM)	RRP and catechin exerted non-competitive inhibition against human 5-LOX (IC_{50} = 15.1 and 2.2 μM, respectively) and rat 5-LOX (IC_{50} = 7.0 and 9.0 μM, respectively)	RRP exerted no effect on COX-1 or COX-2 activity up to 500 μM	[101]

Abbreviations: **AA**, arachidonic acid; **ADP**, adenosine diphosphate; **APF**, 2-[6-(4′-amino)phenoxy-3H-xanthen-3-on-9-yl]benzoic acid; **BMCMCs**, canine bone marrow derived cultured mast cells; **BMMC**, mice bone marrow-derived mast cells; **cAMP**, cyclic adenosine monophosphate; **CAPE**, caffeic acid phenethyl ester; **CLP**, coactosin-like protein; **ConA**, concanavalin A; **COX**, cyclooxygenase; **CpG**, unmethylated CpG motifs of bacteria DNA; **cPLA2**, cytoplasmic phospholipase-2; **Cys-LTs**, cysteinyl leukotrienes; **DNP-HAS**, dinitrophenyl human serum albumin; **DNP-IgE**, dinitrophenyl immunoglobulin E; **DPE**, 2-(3,4-dihydroxy-phenyl)-ethanol; **EGCG**, epigallocatechin gallate; **FLG**, flagellin; **fMLP**, formyl methionyl leucyl phenylalamine; **HETE**, hydroxyeicosatetraenoic acid; **HHT**, hydroxy-5,8,10-heptadecatetraenoic acid; **HKE_2**, hemiketal E_2; **HKD_2**, hemiketal D_2; **HODE**, hydroxyoctadecadienoic acid; **HO-1**, hemeoxygenase-1; **HPETE**, hydroxyperoxyeicosatetraenoic acid; **iNOS**, inducible nitric oxide synthase; **KL**, c-kit ligand; **LOX**, lipoxygenase; **LOX-1**, lectin-like oxidized low-density lipoprotein receptor-1; **LPS**, lipopolysaccharide; **LT**, leukotrienes; **MAPK**, mitogen activated protein kinase; **MK2**, mitogen-activated protein kinase-activated protein kinase2; **mPGES**, microsomal prostaglandin E synthase; **MPO**, myeloperoxidase; **MQ**, 3′-*O*-methylquercetin; **MQG**, 3′-*O*-methylquercetin-3-*O*-glucuronide; **Myr-3-glur**; myricetin-3-*O*-β-D-glucuronide; **NDGA**, nordihydroguaiaretic acid; **NF-κB**, nuclear factor kappa-light-chain-enhancer of activated B cells; **NO**, nitric oxide; **OAG**, 1-oleoyl-2-acetylglycerol; **ox-LDL**, oxidized low density lipoprotein; **p12-LOX**, porcine leukocyte-like 12 lipoxygenase; **PAM**, bacterial lipoprotein mimic palmitoly-3-cysteine–serine–lysine-4; **PBMCs**, peripheral blood mononuclear cells; **PC**, phosphatidil coline; **PG**, prostaglandins; **PLA_2**, phospholipase-2; **PMA**, phorbol 12-myristate 13-acetate; **PMNLs**, polymorphonuclear leukocytes; **QG**, quercetin-3-*O*-glucuronide; **QS**, quercetin-3′-*O*-sulfate; **ROS**, reactive oxygen species; **RRP**, red-kerneled rice proanthocyanidin; **RSV**, resveratrol; **THC**, tetrahydrocurcumin; **TLR**, toll-like receptor; **TNF-α**, tumor necrosis factor alpha; **Tr-LTB_4**, trans-LTB_4; **Trp**, tryptophan; **TxB_2**, thromboxane B_2; **Uro**, urolithins;

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