Bone & Joint Research

Supplementary Material

10.1302/2046-3758.115.BJR-2021-0380.R1

Table i. Coefficient genes of auraptene obtained from PubChem.

Gene names	Articles	Journal
Tumor Necrosis Factor	Comparative evaluation of the protective effects of oral administration of auraptene and umbelliprenin against Complete Freund's adjuvant (CFA)-induced chronic inflammation with polyarthritis in rats	Biomed Pharmacother 2021;139:111635
	Anti-oxidant and anti-inflammatory effects of auraptene on phytohemagglutinin (PHA)-induced inflammation in human lymphocytes	Pharmacol Rep 2021;73(1):154-162
	Computational discovery and experimental verification of farnesoid X receptor agonist auraptene to protect against cholestatic liver injury	Biochem Pharmacol 2017;146:127-138
	Hepatoprotection of auraptene from peels of citrus fruits against thioacetamide-induced hepatic fibrosis in mice by activating farnesoid X receptor	Food Funct 2018;9(5):2684-2694
	Auraptene attenuates gastritis via reduction of Helicobacter pylori colonization and pro-inflammatory mediator production in C57BL/6 mice	J Med Food 2012;15(7):658-63
Mitogen-Activated Protein Kinase Erk-A	Suppression of Human Platelet Activation via Integrin αIIbβ3 Outside-In Independent Signal and Reduction of the Mortality in Pulmonary Thrombosis by Auraptene	Int J Mol Sci 2019;20(22):5585
	Citrus Auraptene Induces Glial Cell Line-Derived Neurotrophic Factor in C6 Cells	Int J Mol Sci 2019;21(1):253

	Stimulation of phosphorylation of ERK and CREB by phellopterin and auraptene isolated from *Citrus junos*	Nat Prod Commun 2014;9(10):1491-1494
	Citrus auraptene targets translation of MMP-7 (matrilysin) via ERK1/2-dependent and mTOR-independent mechanism	FEBS Lett 2006;580(22):5288-5294
	Zingiberaceous and citrus constituents, 1'-acetoxychavicol acetate, zerumbone, auraptene, and nobiletin, suppress lipopolysaccharide-induced cyclooxygenase-2 expression in RAW264.7 murine macrophages through different modes of action	J Nutr 2005;135(12 Suppl):2987S-2992S
Mitogen-Activated Protein Kinase 3	Suppression of Human Platelet Activation via Integrin αIIbβ3 Outside-In Independent Signal and Reduction of the Mortality in Pulmonary Thrombosis by Auraptene	Int J Mol Sci 2019;20(22):5585
	The Coumarin Derivative 5'-Hydroxy Auraptene Suppresses Osteoclast Differentiation via Inhibiting MAPK and c-Fos/NFATc1 Pathways	Biomed Res Int 2019;2019:9395146
	Neurotrophic effect of citrus auraptene: neuritogenic activity in PC12 cells	Int J Mol Sci 2012;13(5):5338-5347
	Citrus auraptene targets translation of MMP-7 (matrilysin) via ERK1/2-dependent and mTOR-independent mechanism	FEBS Lett 2006;580(22):5288-5294
	Suppression of CD74 expression and Helicobacter pylori adhesion by auraptene targeting serum starvation-activated ERK1/2 in NCI-N87 gastric carcinoma cells	Biosci Biotechnol Biochem 2010;74(5):1018-1024
Artemin	Citrus Auraptene Induces Glial Cell Line-Derived Neurotrophic Factor in C6 Cells	Int J Mol Sci 2019;21(1):253
	Citrus Auraptene Induces Expression of Brain-Derived Neurotrophic Factor in Neuro2a Cells	Molecules 2020;25(5):1117
	[Search for Neuroprotective Compounds -From 4-Methycatechol to Citrus Compounds]	Yakugaku Zasshi 2021;141(1):67-79
	Isolation and Characterization of Neuroprotective Components from Citrus Peel and Their Application as Functional Food	Chem Pharm Bull (Tokyo) 2021;69(1):2-10

	[Effects of Bioactive Substances from Citrus on the Central Nervous System and Utilization as Food Material]	Yakugaku Zasshi 2015;135(10):1153-1159
Cytochrome P450 Family 8 Subfamily B Member 1	Computational discovery and experimental verification of farnesoid X receptor agonist auraptene to protect against cholestatic liver injury	Biochem Pharmacol 2017;146:127-138
	Hepatoprotection of auraptene from peels of citrus fruits against thioacetamide-induced hepatic fibrosis in mice by activating farnesoid X receptor	Food Funct 2018;9(5):2684-2694
	Hepatoprotection of auraptene from the peels of citrus fruits against 17α-ethinylestradiol-induced cholestasis in mice by activating farnesoid X receptor	Food Funct 2019;10(7):3839-3850
Nad(P)H Dehydrogenase (Quinone)	Citrus auraptene inhibits chemically induced colonic aberrant crypt foci in male F344 rats	Carcinogenesis 1997;18(11):2155-2161
	Chemoprevention of 4-nitroquinoline 1-oxide-induced oral carcinogenesis by citrus auraptene in rats	Carcinogenesis 1998;19(3):425-431
	Citrus auraptene exerts dose-dependent chemopreventive activity in rat large bowel tumorigenesis: the inhibition correlates with suppression of cell proliferation and lipid peroxidation and with induction of phase II drug-metabolizing enzymes	Cancer Res. 1998;58(12):2550-2556
	Comparison of citrus coumarins on carcinogen-detoxifying enzymes in Nrf2 knockout mice	Toxicol Lett 2009;185(3):180-186
Nuclear Receptor Subfamily 1 Group H Member 4	Computational discovery and experimental verification of farnesoid X receptor agonist auraptene to protect against cholestatic liver injury	Biochem Pharmacol 2017;146:127-138
	Hepatoprotection of auraptene from peels of citrus fruits against thioacetamide-induced hepatic fibrosis in mice by activating farnesoid X receptor	Food Funct 2018;9(5):2684-2694
	Hepatoprotection of auraptene from the peels of citrus fruits against 17α-ethinylestradiol-induced cholestasis in mice by activating farnesoid X receptor	Food Funct 2019;10(7):3839-3850
	Nelumal A, the active principle from *Ligularia nelumbifolia*, is a novel farnesoid X receptor agonist	Bioorg Med Chem Lett 2012;22(9):3130-3135

Akt Serine/Threonine Kinase 1	Suppression of Human Platelet Activation via Integrin αIIbβ3 Outside-In Independent Signal and Reduction of the Mortality in Pulmonary Thrombosis by Auraptene	Int J Mol Sci 2019;20(22):5585
	Coadministration of auraptene and radiotherapy; a novel modality against colon carcinoma cells in vitro and in vivo	Int J Radiat Biol 2020;96(8):1051-1059
	Auraptene, a Major Compound of Supercritical Fluid Extract of Phalsak (Citrus Hassaku Hort ex Tanaka), Induces Apoptosis through the Suppression of mTOR Pathways in Human Gastric Cancer SNU-1 Cells	Evid Based Complement Alternat Med 2015;2015:402385
	Citrus auraptene targets translation of MMP-7 (matrilysin) via ERK1/2-dependent and mTOR-independent mechanism	FEBS Lett 2006;580(22):5288-5294
	Zingiberaceous and citrus constituents, 1'-acetoxychavicol acetate, zerumbone, auraptene, and nobiletin, suppress lipopolysaccharide-induced cyclooxygenase-2 expression in RAW264.7 murine macrophages through different modes of action	J Nutr 2005;135(12 Suppl):2987S-2992S
Inositol-3-Phosphate Synthase	Dietary administration with prenyloxycoumarins, auraptene and collinin, inhibits colitis-related colon carcinogenesis in mice	Int J Cancer 2006;118(12):2936-2942
	Cancer-preventive anti-oxidants that attenuate free radical generation by inflammatory cells	Biol Chem 2006;387(4):387-392
	Anti-inflammatory terpenylated coumarins from the leaves of *Zanthoxylum schinifolium* with α-glucosidase inhibitory activity	J Nat Med 2016;70(2):276-281
	Development of a quantitative bioassay to assess preventive compounds against inflammation-based carcinogenesis	Nitric Oxide 2011;25(2):183-194
	Effects of selected food factors with chemopreventive properties on combined lipopolysaccharide- and interferon-gamma-induced IkappaB (IκB) degradation in RAW264.7 macrophages	Cancer Lett 2003;195(1):17-25
Interleukin 4	Comparative evaluation of the protective effects of oral administration of auraptene and	Biomed Pharmacother 2021;139:111635

	umbelliprenin against CFA-induced chronic inflammation with polyarthritis in rats	
	Antitumor effects of Auraptene in 4T1 tumor-bearing Balb/c mice	Horm Mol Biol Clin Investig 2021
	Auraptene regulates Th1/Th2/TReg balances, NF-κB nuclear localization and nitric oxide production in normal and Th2 provoked situations in human isolated lymphocytes	Phytomedicine 2018;43:1-10
	Auraptene has the inhibitory property on murine T lymphocyte activation	Eur J Pharmacol 2015;750:8-13
	Immunomodulatory action of citrus auraptene on macrophage functions and cytokine production of lymphocytes in female BALB/c mice	Carcinogenesis 1999;20(8):1471-1476
Solute Carrier Family 10 Member 1	Computational discovery and experimental verification of farnesoid X receptor agonist auraptene to protect against cholestatic liver injury	Biochem Pharmacol 2017;146:127-138
	Hepatoprotection of auraptene from peels of citrus fruits against thioacetamide-induced hepatic fibrosis in mice by activating farnesoid X receptor	Food Funct 2018;9(5):2684-2694
	Hepatoprotection of auraptene from the peels of citrus fruits against 17α-ethinylestradiol-induced cholestasis in mice by activating farnesoid X receptor	Food Funct 2019;10(7):3839-3850
Cytochrome P450 Family 7 Subfamily A Member 1	Computational discovery and experimental verification of farnesoid X receptor agonist auraptene to protect against cholestatic liver injury	Biochem Pharmacol 2017;146:127-138
	Hepatoprotection of auraptene from peels of citrus fruits against thioacetamide-induced hepatic fibrosis in mice by activating farnesoid X receptor	Food Funct 2018;9(5):2684-2694
	Hepatoprotection of auraptene from the peels of citrus fruits against 17α-ethinylestradiol-induced cholestasis in mice by activating farnesoid X receptor	Food Funct 2019;10(7):3839-3850
Proliferating Cell Nuclear Antigen	Dietary administration with prenyloxycoumarins, auraptene and collinin, inhibits colitis-related colon carcinogenesis in mice	Int J Cancer 2006;118(12):2936-2942
	Suppression of N-nitrosomethylbenzylamine-induced	J Exp Clin Cancer Res. 2000;19(1):45-52

	rat esophageal tumorigenesis by dietary feeding of auraptene	
	Suppression by citrus auraptene of phorbol ester-and endotoxin-induced inflammatory responses: role of attenuation of leukocyte activation	Carcinogenesis 2000;21(10):1843-1850
	Chemopreventive effects of coumaperine from pepper on the initiation stage of chemical hepatocarcinogenesis in the rat	Jpn J Cancer Res 2000;91(7):674-680
	Coadministration of auraptene and radiotherapy; a novel modality against colon carcinoma cells in vitro and in vivo	Int J Radiat Biol 2020;96(8):1051-1059
Cyclin-D1-1	Auraptene-induced cytotoxicity mechanisms in human malignant glioblastoma (U87) cells: role of reactive oxygen species (ROS)	EXCLI J 2019;18:576-590
	Effects of Auraptene on IGF-1 Stimulated Cell Cycle Progression in the Human Breast Cancer Cell Line, MCF-7	Int J Breast Cancer 2012;2012:502092
	Citrus auraptene suppresses cyclin D1 and significantly delays N-methyl nitrosourea induced mammary carcinogenesis in female Sprague-Dawley rats	BMC Cancer 2009;9:259
Mitogen-Activated Protein Kinase	Suppression of Human Platelet Activation via Integrin αIIbβ3 Outside-In Independent Signal and Reduction of the Mortality in Pulmonary Thrombosis by Auraptene	Int J Mol Sci 2019;20(22):5585
	Citrus Auraptene Induces Glial Cell Line-Derived Neurotrophic Factor in C6 Cells	Int J Mol Sci 2019;21(1):253
	Auraptene increases the production of amyloid-β via c-Jun N-terminal kinase-dependent activation of γ-secretase	J Alzheimers Dis 2015;43(4):1215-1228
	Apoptogenic activity of auraptene of *Zanthoxylum schinifolium* toward human acute leukemia Jurkat T cells is associated with ER stress-mediated caspase-8 activation that stimulates mitochondria-dependent or -independent caspase cascade	Carcinogenesis 2007;28(6):1303-1313
	Zingiberaceous and citrus constituents, 1'-acetoxychavicol acetate, zerumbone, auraptene, and nobiletin, suppress lipopolysaccharide-induced	J Nutr 2005;135(12 Suppl):2987S-2992S

	cyclooxygenase-2 expression in RAW264.7 murine macrophages through different modes of action	
Xenobiotic-Transporting ATPase	Citrus auraptene induces drug efflux transporter P-glycoprotein expression in human intestinal cells	Food Funct 2020;11(6):5017-5023
	[Chemical study of citrus plants in the search for cancer chemopreventive agents]	Yakugaku Zasshi 2005;125(3):231-254
	Effects of chemopreventive citrus phytochemicals on human P-glycoprotein and multidrug resistance protein 1	Eur J Pharmacol 2008;600(1-3):45-49
	Polymethoxylated flavones and other phenolic derivates from citrus in their inhibitory effects on P-glycoprotein-mediated transport of talinolol in Caco-2 cells	J Agric Food Chem 2007;55(7):2563-2568
Nuclear Factor Kappa B Subunit 1	Zingiberaceous and citrus constituents, 1'-acetoxychavicol acetate, zerumbone, auraptene, and nobiletin, suppress lipopolysaccharide-induced cyclooxygenase-2 expression in RAW264.7 murine macrophages through different modes of action	J Nutr 2005;135(12 Suppl):2987S-2992S
	Cancer-preventive anti-oxidants that attenuate free radical generation by inflammatory cells	
	Effects of ATRA combined with citrus and ginger-derived compounds in human SCC xenografts	BMC Cancer 2010;10:394
	Citrus nobiletin suppresses bone loss in ovariectomized ddY mice and collagen-induced arthritis in DBA/1J mice: possible involvement of receptor activator of NF-kappaB ligand (RANKL)-induced osteoclastogenesis regulation	Biofactors 2007;30(3):179-192
Mitogen-Activated Protein Kinase 8	Suppression of Human Platelet Activation via Integrin αIIbβ3 Outside-In Independent Signal and Reduction of the Mortality in Pulmonary Thrombosis by Auraptene	Int J Mol Sci 2019;20(22):5585
	The Coumarin Derivative 5'-Hydroxy Auraptene Suppresses Osteoclast Differentiation via Inhibiting MAPK and c-Fos/NFATc1 Pathways	Biomed Res Int 2019;2019:9395146
	Zingiberaceous and citrus constituents, 1'-acetoxychavicol acetate, zerumbone, auraptene, and	J Nutr 2005;135(12 Suppl):2987S-2992S

	nobiletin, suppress lipopolysaccharide-induced cyclooxygenase-2 expression in RAW264.7 murine macrophages through different modes of action	
	Cancer-preventive anti-oxidants that attenuate free radical generation by inflammatory cells	Biol Chem 2006;387(4):387-392
Acetylcholinesterase	Comparison of the chemical constituents of raw Fructus Aurantii and Fructus Aurantii stir-baked with bran, and the biological effects of auraptene	J Ethnopharmacol 2021;269:113721
	Auraptene consolidates memory, reverses scopolamine-disrupted memory in passive avoidance task, and ameliorates retention deficits in mice	Iran J Basic Med Sci 2015;18(10):1014-1019
	Combination of bioautography with HPTLC-MS/NMR: a fast identification of acetylcholinesterase inhibitors from galbanum(†)	Phytochem Anal 2013;24(4):395-400
	Inhibition of acetylcholinesterase activity by essential oil from Citrus paradisi	Nat Prod Lett 2001;15(3):205-210
Sulfotransferase Family 2a Member 1	Computational discovery and experimental verification of farnesoid X receptor agonist auraptene to protect against cholestatic liver injury	Biochem Pharmacol 2017;146:127-138
	Hepatoprotection of auraptene from the peels of citrus fruits against 17α-ethinylestradiol-induced cholestasis in mice by activating farnesoid X receptor	Food Funct 2019;10(7):3839-3850
CD74 Molecule	Auraptene attenuates gastritis via reduction of Helicobacter pylori colonization and pro-inflammatory mediator production in C57BL/6 mice	J Med Food 2012;15(7):658-663
	Suppression of CD74 expression and Helicobacter pylori adhesion by auraptene targeting serum starvation-activated ERK1/2 in NCI-N87 gastric carcinoma cells	Biosci Biotechnol Biochem 2010;74(5):1018-1024
CD44 Molecule (Indian Blood Group)	Coadministration of auraptene and radiotherapy; a novel modality against colon carcinoma cells in vitro and in vivo	Int J Radiat Biol 2020;96(8):1051-1059
	Auraptene Attenuates Malignant Properties of Esophageal Stem-Like Cancer Cells	Technol Cancer Res Treat 2017;16(4):519-527

	Synergy between Auraptene, Ionizing Radiation, and Anticancer Drugs in Colon Adenocarcinoma Cells	Phytother Res 2017;31(9):1369-1375
Nad(+) ADP-ribosyltransferase	Auraptene Induces Apoptosis via Myeloid Cell Leukemia 1-Mediated Activation of Caspases in PC3 and DU145 Prostate Cancer Cells	Phytother Res 2017;31(6):891-898
	Auraptene, a Major Compound of Supercritical Fluid Extract of Phalsak (Citrus Hassaku Hort ex Tanaka), Induces Apoptosis through the Suppression of mTOR Pathways in Human Gastric Cancer SNU-1 Cells	Evid Based Complement Alternat Med 2015;2015:402385
	Apoptogenic activity of auraptene of *Zanthoxylum schinifolium* toward human acute leukemia Jurkat T cells is associated with ER stress-mediated caspase-8 activation that stimulates mitochondria-dependent or -independent caspase cascade	Carcinogenesis 2007;28(6):1303-1313
Cytochrome P450 Family 3 Subfamily A Member 4	Binding of furanocoumarins in grapefruit juice to Aspergillus niger hyphae	Appl Microbiol Biotechnol 2008;78(3):401-407
	Minor furanocoumarins and coumarins in grapefruit peel oil as inhibitors of human cytochrome P450 3A4	J Nat Prod 2009;72(9):1702-1704
	Distribution of furanocoumarins in grapefruit juice fractions	J Agric Food Chem 2005;53(13):5158-5163
ATP Binding Cassette Subfamily B Member 1	Citrus auraptene induces drug efflux transporter P-glycoprotein expression in human intestinal cells	Food Funct 2020;11(6):5017-5023
	Effects of chemopreventive citrus phytochemicals on human P-glycoprotein and multidrug resistance protein 1	Eur J Pharmacol 2008;600(1-3):45-49
	Polymethoxylated flavones and other phenolic derivates from citrus in their inhibitory effects on P-glycoprotein-mediated transport of talinolol in Caco-2 cells	J Agric Food Chem 2007;55(7):2563-2568
Jun Proto-Oncogene, AP-1 Transcription Factor Subunit	Zingiberaceous and citrus constituents, 1'-acetoxychavicol acetate, zerumbone, auraptene, and nobiletin, suppress lipopolysaccharide-induced cyclooxygenase-2 expression in RAW264.7 murine macrophages through different modes of action	J Nutr 2005;135(12 Suppl):2987S-2992S
	Citrus nobiletin suppresses bone loss in ovariectomized ddY mice and	Biofactors 2007;30(3):179-192

	collagen-induced arthritis in DBA/1J mice: possible involvement of receptor activator of NF-kappaB ligand (RANKL)-induced osteoclastogenesis regulation	
	Cell proliferation in cancer prevention; effects of preventive agents on estrogen-related endometrial carcinogenesis model and on an in vitro model in human colorectal cells	Mutat Res 2001;480-481:201-207
Interferon Lambda Receptor 1	Auraptene has the inhibitory property on murine T lymphocyte activation	Eur J Pharmacol 2015;750:8-13
	Immunomodulatory action of citrus auraptene on macrophage functions and cytokine production of lymphocytes in female BALB/c mice	Carcinogenesis 1999;20(8):1471-1476
	Methyl galbanate, a novel inhibitor of nitric oxide production in mouse macrophage RAW264.7 cells	J Nat Med 2011;65(2):353-359
	Effects of selected food factors with chemopreventive properties on combined lipopolysaccharide- and interferon-gamma-induced IkappaB degradation in RAW264.7 macrophages	Cancer Lett 2003;195(1):17-25
Brain Derived Neurotrophic Factor	Citrus Auraptene Induces Expression of Brain-Derived Neurotrophic Factor in Neuro2a Cells	Molecules 2020;25(5):1117
	[Search for Neuroprotective Compounds -From 4-Methycatechol to Citrus Compounds]	Yakugaku Zasshi 2021;141(1):67-79
	Modulation of neurotrophic signaling pathways by polyphenols	Drug Des Devel Ther 2015;10:23-42
Matrix Metallopeptidase 7	Citrus auraptene targets translation of MMP-7 (matrilysin) via ERK1/2-dependent and mTOR-independent mechanism	FEBS Lett 2006;580(22):5288-5294
	Auraptene decreases the activity of matrix metalloproteinases in dextran sulfate sodium-induced ulcerative colitis in ICR mice	Biosci Biotechnol Biochem 2006;70(12):3062-3065
Acyl-Coa Oxidase	Auraptene, a citrus fruit compound, regulates gene expression as a PPARalpha agonist in HepG2 hepatocytes	Biofactors 2008;33(1):25-32
	Effects of citrus auraptene (7-geranyloxycoumarin) on hepatic lipid metabolism in vitro and in vivo	J Agric Food Chem 2010;58(16):9028-9032

Mitogen-Activated Protein Kinase 14	Suppression of Human Platelet Activation via Integrin αIIbβ3 Outside-In Independent Signal and Reduction of the Mortality in Pulmonary Thrombosis by Auraptene	Int J Mol Sci 2019;20(22):5585
	Auraptene suppresses inflammatory responses in activated RAW264 macrophages by inhibiting p38 mitogen-activated protein kinase activation	Mol Nutr Food Res 2013;57(7):1135-1144
	Citrus nobiletin suppresses bone loss in ovariectomized ddY mice and collagen-induced arthritis in DBA/1J mice: possible involvement of receptor activator of NF-kappaB ligand (RANKL)-induced osteoclastogenesis regulation	Biofactors 2007;30(3):179-192
Catenin Beta 1	Citrus auraptene suppresses azoxymethane-induced colonic preneoplastic lesions in C57BL/KsJ-db/db mice	Nutr Cancer 2007;58(1):75-84
	Suppression of beta-catenin mutation by dietary exposure of auraptene, a citrus antioxidant, in N,N-diethylnitrosamine-induced hepatocellular carcinomas in rats	Oncol Rep 2005;14(2):345-351
	Aggressive mammary carcinoma progression in Nrf2 knockout mice treated with 7,12-dimethylbenz[a]anthracene	BMC Cancer 2010;10:540
Metallothionein-1	pH-Responsive Fluorescence Enhanced Nanogel for Targeted Delivery of AUR and CDDP Against Breast Cancer	Int J Nanomedicine 2020;15:8369-8382
	Oxyprenylated Phenylpropanoids Bind to MT1 Melatonin Receptors and Inhibit Breast Cancer Cell Proliferation and Migration	J Nat Prod 2017;80(12):3324-3329
Prostaglandin-Endoperoxide Synthase 2	Anti-inflammatory and neuroprotective effects of auraptene, a citrus coumarin, following cerebral global ischemia in mice	Eur J Pharmacol 2013;699(1-3):118-123
	Anti-inflammatory effect of auraptene extracted from trifoliate orange (*Poncirus trifoliate*) on LPS-stimulated RAW 264.7 cells	Inflammation 2013;36(6):1525-1532
	Zingiberaceous and citrus constituents, 1'-acetoxychavicol acetate, zerumbone, auraptene, and nobiletin, suppress lipopolysaccharide-induced	J Nutr 2005;135(12 Suppl):2987S-2992S

	cyclooxygenase-2 expression in RAW264.7 murine macrophages through different modes of action	
C-X-C Motif Chemokine Ligand 8	The plant coumarins auraptene and lacinartin as potential multifunctional therapeutic agents for treating periodontal disease	BMC Complement Altern Med 2012;12:80
	Anti-inflammatory and wound healing potential of citrus auraptene	J Med Food 2013;16(10):961-964
	Suppression of CD74 expression and Helicobacter pylori adhesion by auraptene targeting serum starvation-activated ERK1/2 in NCI-N87 gastric carcinoma cells	Biosci Biotechnol Biochem 2010;74(5):1018-1024
Beta-Secretase	Auraptene increases the production of amyloid-β via c-Jun N-terminal kinase-dependent activation of γ-secretase	J Alzheimers Dis 2015;43(4):1215-1228
	Auraptene consolidates memory, reverses scopolamine-disrupted memory in passive avoidance task, and ameliorates retention deficits in mice	Iran J Basic Med Sci 2015;18(10):1014-1019
Regulatory Protein Gal4	Auraptene, a citrus fruit compound, regulates gene expression as a PPARalpha agonist in HepG2 hepatocytes	Biofactors 2008;33(1):25-32
	Effects of naturally occurring coumarins on hepatic drug-metabolizing enzymes in mice	Toxicol Appl Pharmacol 2008;232(2):337-350
Nuclear Receptor Subfamily 1 Group I Member 2	Citrus auraptene induces drug efflux transporter P-glycoprotein expression in human intestinal cells	Food Funct 2020;11(6):5017-5023
	Effects of naturally occurring coumarins on hepatic drug-metabolizing enzymes in mice	Toxicol Appl Pharmacol 2008;232(2):337-350
Glial Cell Derived Neurotrophic Factor	Citrus Auraptene Induces Glial Cell Line-Derived Neurotrophic Factor in C6 Cells	Int J Mol Sci 2019;21(1):253
	Citrus Auraptene Induces Expression of Brain-Derived Neurotrophic Factor in Neuro2a Cells	Molecules 2020;25(5):1117
Watasenia-Luciferin 2-Monooxygenase	Citrus auraptene acts as an agonist for PPARs and enhances adiponectin production and MCP-1 reduction in 3T3-L1 adipocytes	Biochem Biophys Res Commun 2008;366(1):219-225
	Effects of ATRA combined with citrus and ginger-derived compounds in human SCC xenografts	BMC Cancer 2010;10:394

	Nelumal A, the active principle from Ligularia nelumbifolia, is a novel farnesoid X receptor agonist	Bioorg Med Chem Lett 2012;22(9):3130-3135
Nfkb Inhibitor Alpha	Zingiberaceous and citrus constituents, 1'-acetoxychavicol acetate, zerumbone, auraptene, and nobiletin, suppress lipopolysaccharide-induced cyclooxygenase-2 expression in RAW264.7 murine macrophages through different modes of action	J Nutr 2005;135(12 Suppl):2987S-2992S
	Cancer-preventive anti-oxidants that attenuate free radical generation by inflammatory cells	Biol Chem 2006;387(4):387-392
Bcl2 Apoptosis Regulator	Auraptene Induces Apoptosis via Myeloid Cell Leukemia 1-Mediated Activation of Caspases in PC3 and DU145 Prostate Cancer Cells	Phytother Res 2017;31(6):891-898
	Cytotoxic effects of auraptene against a human malignant glioblastoma cell line	Avicenna J Phytomed 2019;9(4):334-346
	Auraptene-induced cytotoxicity mechanisms in human malignant glioblastoma (U87) cells: role of reactive oxygen species (ROS)	EXCLI J 2019;18:576-590
TNF Superfamily Member 11	The Coumarin Derivative 5'-Hydroxy Auraptene Suppresses Osteoclast Differentiation via Inhibiting MAPK and c-Fos/NFATc1 Pathways	Biomed Res Int 2019;2019:9395146
	Citrus nobiletin suppresses bone loss in ovariectomized ddY mice and collagen-induced arthritis in DBA/1J mice: possible involvement of receptor activator of NF-kappaB ligand (RANKL)-induced osteoclastogenesis regulation	Biofactors 2007;30(3):179-192
Caspase-3	Coadministration of auraptene and radiotherapy; a novel modality against colon carcinoma cells in vitro and in vivo	Int J Radiat Biol 2020;96(8):1051-1059
	Auraptene Induces Apoptosis via Myeloid Cell Leukemia 1-Mediated Activation of Caspases in PC3 and DU145 Prostate Cancer Cells	Phytother Res 2017;31(6):891-898
	Auraptene, a Major Compound of Supercritical Fluid Extract of Phalsak (Citrus Hassaku Hort ex Tanaka), Induces Apoptosis through the Suppression of mTOR Pathways in Human Gastric Cancer SNU-1 Cells	Evid Based Complement Alternat Med 2015;2015:402385

Ornithine Decarboxylase	Citrus auraptene inhibits chemically induced colonic aberrant crypt foci in male F344 rats	Carcinogenesis 1997;18(11):2155-2161
	Citrus auraptene exerts dose-dependent chemopreventive activity in rat large bowel tumorigenesis: the inhibition correlates with suppression of cell proliferation and lipid peroxidation and with induction of phase II drug-metabolizing enzymes	Cancer Res. 1998;58(12):2550-2556
Urease	Auraptene attenuates gastritis via reduction of Helicobacter pylori colonization and pro-inflammatory mediator production in C57BL/6 mice	J Med Food 2012;15(7):658-63
	Suppression of CD74 expression and Helicobacter pylori adhesion by auraptene targeting serum starvation-activated ERK1/2 in NCI-N87 gastric carcinoma cells	Biosci Biotechnol Biochem 2010;74(5):1018-1024
Corticostatin-3	Cytotoxic effects of auraptene against a human malignant glioblastoma cell line	Avicenna J Phytomed 2019;9(4):334-346
	Citrus auraptene acts as an agonist for PPARs and enhances adiponectin production and MCP-1 reduction in 3T3-L1 adipocytes	Biochem Biophys Res Commun 2008;366(1):219-225
Protein Kinase X-Linked	Citrus Auraptene Induces Glial Cell Line-Derived Neurotrophic Factor in C6 Cells	Int J Mol Sci 2019;21(1):253
	Behavioral and molecular effects of intrahippocampal infusion of auraptene, resveratrol, and curcumin on H-89-induced deficits on spatial memory acquisition and retention in Morris water maze	Hum Exp Toxicol 2019;38(7):775-784
	[Effects of Bioactive Substances from Citrus on the Central Nervous System and Utilization as Food Material]	Yakugaku Zasshi 2015;135(10):1153-1159
Acid Phosphatase	Immunomodulatory action of citrus auraptene on macrophage functions and cytokine production of lymphocytes in female BALB/c mice	Carcinogenesis 1999;20(8):1471-1476
	Citrus nobiletin suppresses bone loss in ovariectomized ddY mice and collagen-induced arthritis in DBA/1J mice: possible involvement of receptor activator of NF-kappaB ligand (RANKL)-induced osteoclastogenesis regulation	Biofactors 2007;30(3):179-192
Caspase 9	Auraptene Induces Apoptosis via Myeloid Cell Leukemia 1-Mediated	Phytother Res 2017;31(6):891-898

	Activation of Caspases in PC3 and DU145 Prostate Cancer Cells	
	Apoptogenic activity of auraptene of *Zanthoxylum schinifolium* toward human acute leukemia Jurkat T cells is associated with ER stress-mediated caspase-8 activation that stimulates mitochondria-dependent or -independent caspase cascade	Carcinogenesis 2007;28(6):1303-1313
Interleukin-6	Anti-oxidant and anti-inflammatory effects of auraptene on phytohemagglutinin (PHA)-induced inflammation in human lymphocytes	Pharmacol Rep 2021;73(1):154-162
	Computational discovery and experimental verification of farnesoid X receptor agonist auraptene to protect against cholestatic liver injury	Biochem Pharmacol 2017;146:127-138
	Anti-inflammatory and wound healing potential of citrus auraptene	J Med Food 2013;16(10):961-964
Nerve Growth Factor	[Search for Neuroprotective Compounds -From 4-Methycatechol to Citrus Compounds]	Yakugaku Zasshi 2021;141(1):67-79
	Modulation of neurotrophic signaling pathways by polyphenols	Drug Des Devel Ther 2015;10:23-42
Golgi Reassembly Stacking Protein 1	Regulation of Human Platelet Activation and Prevention of Arterial Thrombosis in Mice by Auraptene through Inhibition of NF-κB Pathway	Int J Mol Sci 2020;21(13):4810
	Zingiberaceous and citrus constituents, 1'-acetoxychavicol acetate, zerumbone, auraptene, and nobiletin, suppress lipopolysaccharide-induced cyclooxygenase-2 expression in RAW264.7 murine macrophages through different modes of action	J Nutr 2005;135(12 Suppl):2987S-2992S
Heme Oxygenase 1	Aggressive mammary carcinoma progression in Nrf2 knockout mice treated with 7,12-dimethylbenz[a]anthracene	BMC Cancer 2010;10:540
	Modulation of neurotrophic signaling pathways by polyphenols	Drug Des Devel Ther 2015;10:23-42
Fos Proto-Oncogene, AP-1 Transcription Factor Subunit	The Coumarin Derivative 5'-Hydroxy Auraptene Suppresses Osteoclast Differentiation via Inhibiting MAPK and c-Fos/NFATc1 Pathways	Biomed Res Int 2019;2019:9395146
	Cell proliferation in cancer prevention; effects of preventive agents on estrogen-related endometrial carcinogenesis model	Mutat Res 2001;480-481:201-207

	and on an in vitro model in human colorectal cells	
Lon Peptidase 1, Mitochondrial	Auraptene Enhances Junction Assembly in Cerebrovascular Endothelial Cells by Promoting Resilience to Mitochondrial Stress through Activation of Antioxidant Enzymes and mtUPR	Antioxidants (Basel) 2021;10(3):475
Solute Carrier Family 49 Member 4	Suppression of mitochondrial respiration with auraptene inhibits the progression of renal cell carcinoma: involvement of HIF-1α degradation	Oncotarget 2015;6(35):38127-38138
Activating Transcription Factor 5	Auraptene Enhances Junction Assembly in Cerebrovascular Endothelial Cells by Promoting Resilience to Mitochondrial Stress through Activation of Antioxidant Enzymes and mtUPR	Antioxidants (Basel) 2021;10(3):475
Microtubule Actin Crosslinking Factor 1	Distribution of furanocoumarins in grapefruit juice fractions	J Agric Food Chem 2005;53(13):5158-5163
Eukaryotic Translation Initiation Factor 4b	Citrus auraptene targets translation of MMP-7 (matrilysin) via ERK1/2-dependent and mTOR-independent mechanism	FEBS Lett 2006;580(22):5288-5294
C-X-C Motif Chemokine Ligand 3	Auraptene-induced cytotoxicity mechanisms in human malignant glioblastoma (U87) cells: role of reactive oxygen species (ROS)	EXCLI J 2019;18:576-590
Coagulation Factor II, Thrombin	Suppression of Human Platelet Activation via Integrin αIIbβ3 Outside-In Independent Signal and Reduction of the Mortality in Pulmonary Thrombosis by Auraptene	Int J Mol Sci 2019;20(22):5585
	Antiplatelet actions of some coumarin compounds isolated from plant sources	Thromb Res 1992;66(5):549-557
Interleukin 2	Comparative evaluation of the protective effects of oral administration of auraptene and umbelliprenin against CFA-induced chronic inflammation with polyarthritis in rats	Biomed Pharmacother 2021;139:111635
	Immunomodulatory action of citrus auraptene on macrophage functions and cytokine production of lymphocytes in female BALB/c mice	Carcinogenesis 1999;20(8):1471-1476
Regulator Of Cell Cycle	Effects of Auraptene on IGF-1 Stimulated Cell Cycle Progression in the Human Breast Cancer Cell Line, MCF-7	Int J Breast Cancer 2012;2012:502092

Cytochrome P450, Family 2, Subfamily B, Polypeptide 10	Effects of naturally occurring coumarins on hepatic drug-metabolizing enzymes in mice	Toxicol Appl Pharmacol 2008;232(2):337-350
Mechanistic Target Of Rapamycin Kinase	Auraptene, a Major Compound of Supercritical Fluid Extract of Phalsak (Citrus Hassaku Hort ex Tanaka), Induces Apoptosis through the Suppression of mTOR Pathways in Human Gastric Cancer SNU-1 Cells	Evid Based Complement Alternat Med 2015;2015:402385
	Citrus auraptene targets translation of MMP-7 (matrilysin) via ERK1/2-dependent and mTOR-independent mechanism	FEBS Lett 2006;580(22):5288-5294
Interleukin 10	Comparative evaluation of the protective effects of oral administration of auraptene and umbelliprenin against CFA-induced chronic inflammation with polyarthritis in rats	Biomed Pharmacother 2021;139:111635
	Auraptene regulates Th1/Th2/TReg balances, NF-κB nuclear localization and nitric oxide production in normal and Th2 provoked situations in human isolated lymphocytes	Phytomedicine 2018;43:1-10
GATA Binding Protein 6	Synergy between Auraptene, Ionizing Radiation, and Anticancer Drugs in Colon Adenocarcinoma Cells	Phytother Res 2017;31(9):1369-1375
PTIP Associated Protein 1	Umbelliprenin from *Ferula szowitsiana* inhibits the growth of human M4Beu metastatic pigmented malignant melanoma cells through cell-cycle arrest in G1 and induction of caspase-dependent apoptosis	Phytomedicine 2008;15(1-2):103-111
CXADR Ig-Like Cell Adhesion Molecule	Effects of naturally occurring coumarins on hepatic drug-metabolizing enzymes in mice	Toxicol Appl Pharmacol 2008;232(2):337-350
Protein Kinase C Theta	Suppression of Human Platelet Activation via Integrin αIIbβ3 Outside-In Independent Signal and Reduction of the Mortality in Pulmonary Thrombosis by Auraptene	Int J Mol Sci 2019;20(22):5585
	Network pharmacology based high throughput screening for identification of multi targeted anti-diabetic compound from traditionally used plants	J Biomol Struct Dyn 2021;1-14
Unspecific Monooxygenase	In vitro absorption and metabolism of a citrus chemopreventive agent, auraptene, and its modifying effects on xenobiotic enzyme activities in mouse livers	Nutr Cancer 2000;36(2):191-199

	Chemopreventive effects of coumaperine from pepper on the initiation stage of chemical hepatocarcinogenesis in the rat	Jpn J Cancer Res 2000;91(7):674-680
Vascular Endothelial Growth Factor A	Suppression of mitochondrial respiration with auraptene inhibits the progression of renal cell carcinoma: involvement of HIF-1α degradation	Oncotarget 2015;6(35):38127-38138
	Effects of selected food phytochemicals in reducing the toxic actions of TCDD and p,p'-DDT in U937 macrophages	Arch Toxicol 2010;84(12):957-966
Oligodendrocyte Transcription Factor 2	Auraptene induces oligodendrocyte lineage precursor cells in a cuprizone-induced animal model of demyelination	Brain Res 2016;1639:28-37
Calpain-2	Apoptogenic activity of auraptene of *Zanthoxylum schinifolium* toward human acute leukemia Jurkat T cells is associated with ER stress-mediated caspase-8 activation that stimulates mitochondria-dependent or -independent caspase cascade	Carcinogenesis 2007;28(6):1303-1313
FMN-Dependent NADH:quinone Oxidoreductase	Antinociceptive properties of the hydroalcoholic extract and the flavonoid rutin obtained from *Polygala paniculata L.* in mice	Basic Clin Pharmacol Toxicol 2009;104(4):306-315
GTPase-Activating Protein Pac-1	Suppression of Human Platelet Activation via Integrin αIIbβ3 Outside-In Independent Signal and Reduction of the Mortality in Pulmonary Thrombosis by Auraptene	Int J Mol Sci 2019;20(22):5585
Peroxiredoxin 1	Aggressive mammary carcinoma progression in Nrf2 knockout mice treated with 7,12-dimethylbenz[a]anthracene	BMC Cancer 2010;10:540
Adam Metallopeptidase Domain 10	Auraptene increases the production of amyloid-β via c-Jun N-terminal kinase-dependent activation of γ-secretase	J Alzheimers Dis 2015;43(4):1215-1228
Tyrosine Protein-Kinase Src-1	Effects of naturally occurring coumarins on hepatic drug-metabolizing enzymes in mice	Toxicol Appl Pharmacol 2008;232(2):337-350
Protein Kinase 2	Zingiberaceous and citrus constituents, 1'-acetoxychavicol acetate, zerumbone, auraptene, and nobiletin, suppress lipopolysaccharide-induced cyclooxygenase-2 expression in	J Nutr 2005;135(12 Suppl):2987S-2992S

	RAW264.7 murine macrophages through different modes of action	
Nuclear Factor, Erythroid 2-Like 2a	Colorectal cancer chemoprevention by 2 beta-cyclodextrin inclusion compounds of auraptene and 4'-geranyloxyferulic acid	Int J Cancer 2010;126(4):830-840
Melan-A	Natural oxyprenylated coumarins are modulators of melanogenesis	Eur J Med Chem 2018;152:274-282
Claudin 5	Auraptene Enhances Junction Assembly in Cerebrovascular Endothelial Cells by Promoting Resilience to Mitochondrial Stress through Activation of Antioxidant Enzymes and mtUPR	Antioxidants (Basel) 2021;10(3):475
11-Beta-Hydroxysteroid Dehydrogenase	Network pharmacology based high throughput screening for identification of multi targeted anti-diabetic compound from traditionally used plants	J Biomol Struct Dyn 2021;1-14
Long-Chain-Fatty-Acid--CoA Ligase	Auraptene, a citrus fruit compound, regulates gene expression as a PPARalpha agonist in HepG2 hepatocytes	Biofactors 2008;33(1):25-32
Dead-Box Helicase 53	Coadministration of auraptene and radiotherapy; a novel modality against colon carcinoma cells in vitro and in vivo	Int J Radiat Biol 2020;96(8):1051-1059
Bcl2 Associated X, Apoptosis Regulator	Auraptene Induces Apoptosis via Myeloid Cell Leukemia 1-Mediated Activation of Caspases in PC3 and DU145 Prostate Cancer Cells	Phytother Res 2017;31(6):891-898
Nuclear Receptor Subfamily 1 Group I Member 3	Effects of naturally occurring coumarins on hepatic drug-metabolizing enzymes in mice	Toxicol Appl Pharmacol 2008;232(2):337-350
Protein Trunk	Modulation of neurotrophic signaling pathways by polyphenols	Drug Des Devel Ther 2015;10:23-42
Carnitine Palmitoyltransferase 1a	Auraptene, a citrus fruit compound, regulates gene expression as a PPARalpha agonist in HepG2 hepatocytes	Biofactors 2008;33(1):25-32
Sirtuin 3	Citrus hassaku Extract Powder Increases Mitochondrial Content and Oxidative Muscle Fibers by Upregulation of PGC-1α in Skeletal Muscle	Nutrients 2021;13(2):497
Eukaryotic Initiation Factor 4a	Citrus auraptene targets translation of MMP-7 (matrilysin) via ERK1/2-dependent and mTOR-independent mechanism	FEBS Lett 2006;580(22):5288-5294

Macrophage Migration Inhibitory Factor	Auraptene attenuates gastritis via reduction of Helicobacter pylori colonization and pro-inflammatory mediator production in C57BL/6 mice	J Med Food 2012;15(7):658-63
Acetyl-CoA Acetyltransferase 1	Auraptene is an inhibitor of cholesterol esterification and a modulator of estrogen receptors	Mol Pharmacol 2010;78(5):827-836
Nuclear Factor Of Activated T Cells 1	The Coumarin Derivative 5'-Hydroxy Auraptene Suppresses Osteoclast Differentiation via Inhibiting MAPK and c-Fos/NFATc1 Pathways	Biomed Res Int 2019;2019:9395146
Bone Morphogenetic Protein 2b	5'-hydroxy Auraptene stimulates osteoblast differentiation of bone marrow-derived mesenchymal stem cells via a BMP-dependent mechanism	J Biomed Sci 2019;26(1):51
Presenilin 1	Auraptene increases the production of amyloid-β via c-Jun N-terminal kinase-dependent activation of γ-secretase	J Alzheimers Dis 2015;43(4):1215-1228
SMAD Family Member 4	5'-hydroxy Auraptene stimulates osteoblast differentiation of bone marrow-derived mesenchymal stem cells via a BMP-dependent mechanism	J Biomed Sci 2019;26(1):51
Ribonuclease A Family Member 3	Antidepressant-like effect of Casimiroa pubescens root extracts	Nat Prod Res 2019;33(17):2526-2530

NOTE: Please save this file locally before filling in the table, DO NOT work on the file within your internet browser as changes will not be saved. Adobe Acrobat Reader (available free here) is recommended for completion.

The ARRIVE guidelines 2.0: author checklist

The ARRIVE Essential 10

These items are the basic minimum to include in a manuscript. Without this information, readers and reviewers cannot assess the reliability of the findings.

Item		Recommendation	Section/line number, or reason for not reporting
Study design	1	For each experiment, provide brief details of study design including:	
		a. The groups being compared, including control groups. If no control group has been used, the rationale should be stated.	Animal experiment
		b. The experimental unit (e.g. a single animal, litter, or cage of animals).	Animal experiment
Sample size	2	a. Specify the exact number of experimental units allocated to each group, and the total number in each experiment. Also indicate the total number of animals used.	Animal experiment
		b. Explain how the sample size was decided. Provide details of any *a priori* sample size calculation, if done.	Animal experiment
Inclusion and exclusion criteria	3	a. Describe any criteria used for including and excluding animals (or experimental units) during the experiment, and data points during the analysis. Specify if these criteria were established *a priori.* If no criteria were set, state this explicitly.	Animal experiment
		b. For each experimental group, report any animals, experimental units or data points not included in the analysis and explain why. If there were no exclusions, state so.	N/A
		c. For each analysis, report the exact value of *n* in each experimental group.	Animal experiment
Randomisation	4	a. State whether randomisation was used to allocate experimental units to control and treatment groups. If done, provide the method used to generate the randomisation sequence.	Animal experiment
		b. Describe the strategy used to minimise potential confounders such as the order of treatments and measurements, or animal/cage location. If confounders were not controlled, state this explicitly.	Animal experiment
Blinding	5	Describe who was aware of the group allocation at the different stages of the experiment (during the allocation, the conduct of the experiment, the outcome assessment, and the data analysis).	Animal experiment
Outcome measures	6	a. Clearly define all outcome measures assessed (e.g. cell death, molecular markers, or behavioural changes).	Figure 3.
		b. For hypothesis-testing studies, specify the primary outcome measure, i.e. the outcome measure that was used to determine the sample size.	Animal experiment
Statistical methods	7	a. Provide details of the statistical methods used for each analysis, including software used.	Statistical analysis
		b. Describe any methods used to assess whether the data met the assumptions of the statistical approach, and what was done if the assumptions were not met.	Statistical analysis
Experimental animals	8	a. Provide species-appropriate details of the animals used, including species, strain and substrain, sex, age or developmental stage, and, if relevant, weight.	Animal experiment
		b. Provide further relevant information on the provenance of animals, health/immune status, genetic modification status, genotype, and any previous procedures.	Animal experiment
Experimental procedures	9	For each experimental group, including controls, describe the procedures in enough detail to allow others to replicate them, including:	Animal experiment
		a. What was done, how it was done and what was used.	Animal experiment
		b. When and how often.	Animal experiment
		c. Where (including detail of any acclimatisation periods).	Animal experiment
		d. Why (provide rationale for procedures).	Animal experiment
Results	10	For each experiment conducted, including independent replications, report:	Statistical analysis
		a. Summary/descriptive statistics for each experimental group, with a measure of variability where applicable (e.g. mean and SD, or median and range).	Figure 3., Figure 6., Figure 7.
		b. If applicable, the effect size with a confidence interval.	

The Recommended Set

These items complement the Essential 10 and add important context to the study. Reporting the items in both sets represents best practice.

Item		Recommendation	Section/line number, or reason for not reporting
Abstract	11	Provide an accurate summary of the research objectives, animal species, strain and sex, key methods, principal findings, and study conclusions.	Abstract
Background	12	a. Include sufficient scientific background to understand the rationale and context for the study, and explain the experimental approach. b. Explain how the animal species and model used address the scientific objectives and, where appropriate, the relevance to human biology.	Introduction Animal experiment
Objectives	13	Clearly describe the research question, research objectives and, where appropriate, specific hypotheses being tested.	Introduction
Ethical statement	14	Provide the name of the ethical review committee or equivalent that has approved the use of animals in this study, and any relevant licence or protocol numbers (if applicable). If ethical approval was not sought or granted, provide a justification.	Introduction
Housing and husbandry	15	Provide details of housing and husbandry conditions, including any environmental enrichment.	Animal experiment
Animal care and monitoring	16	a. Describe any interventions or steps taken in the experimental protocols to reduce pain, suffering and distress. b. Report any expected or unexpected adverse events. c. Describe the humane endpoints established for the study, the signs that were monitored and the frequency of monitoring. If the study did not have humane endpoints, state this.	Animal experiment Animal experiment N/A
Interpretation/ scientific implications	17	a. Interpret the results, taking into account the study objectives and hypotheses, current theory and other relevant studies in the literature. b. Comment on the study limitations including potential sources of bias, limitations of the animal model, and imprecision associated with the results.	Introduction Strengths and limitations
Generalisability/ translation	18	Comment on whether, and how, the findings of this study are likely to generalise to other species or experimental conditions, including any relevance to human biology (where appropriate).	N/A
Protocol registration	19	Provide a statement indicating whether a protocol (including the research question, key design features, and analysis plan) was prepared before the study, and if and where this protocol was registered.	Animal experiment
Data access	20	Provide a statement describing if and where study data are available.	Funding information
Declaration of interests	21	a. Declare any potential conflicts of interest, including financial and non-financial. If none exist, this should be stated. b. List all funding sources (including grant identifier) and the role of the funder(s) in the design, analysis and reporting of the study.	Funding information Funding information