

Supplementary Material

Flavonoids with Anti-angiogenesis Function in Cancer

Table S1. Antiangiogenic molecular mechanisms of different flavonoids.

Type	Compounds (No.)	Cancer moder/cell line	Event	Mechanism	Reference
Flavone	Scutellarin(1)	HUVECs, CAM; colon cancer HCT116, LOVO, SW480 and HT29 cells	↓Tube formation and ephrinb2	Targeting ephrinb2 signaling	[1]
Flavone	Scutellarin(1)	Human oral cancer SAS cells	↓MMP-2, MMP-9, integrin $\alpha v \beta 6$	Possibly regulating transcription factor AP-1	[2]
Flavone	Scutellarin(1)	Melanoma A375 cells	↓p-Akt, p-mTOR, VEGF-A, MMP-2, MMP-9	Inhibiting PI3K/Akt/mTOR pathway	[3]
Flavone	Tricin(2)	HUVECs	↓VEGFR2 and VEGF	Reducing ROS; inhibiting HIF-1 α accumulation	[4]
Flavone	Chrysin(3)	Prostate cancer DU145 cells	↓HIF-1 α	Regulating PI3K/Akt signaling	[5]
Flavone	Chrysin(3)	HUVECs	↓gp130, sIL-6R, phosphorylated JAK1 and STAT3, VEGF	Downregulating JAK1/STAT3 pathway	[6]
Flavone	Chrysin(3)	HUVECs, CAM	↓VEGF, VEGFR2, L-6, IL-6R	Downregulating VEGF/VEGFR2 expression	[7]
Flavone	TTF1(4)	HepG-2-transplanted nude mice	↓VEGF, KDR, bFGF, COX-2, HIF-1 α	Downregulating VEGF, KDR, bFGF, HIF-1 α and COX-2	[8]
Flavone	Luteonin(5)	Breast cancer MCF-7 cells	↓AEG-1, MMP-2	Downregulating AEG-1 and MMP-2	[9]
Flavone	Luteonin(5)	BGC-823-transplanted nude mice	↓VEGF-A, MMP-9	Stimulating immune response and down-regulating VEGF-A and MMP-9	[10]
Flavone	Luteonin(5)	HUVECs, prostate cancer PC-3 cells	↓VEGFR2, Akt, ERK, mTOR, P70S6K, MMP-2 and MMP-9	Inhibiting AKT/ERK/mTOR/P70S6K/MMPs pathway	[11]
Flavone	Luteonin(5)	Human pancreatic carcinoma PANC-1, CoLo-357, BxPC-3 cells	↓VEGF secretion and expression; ↑phosphorylation level of JNK	Elevating JNK phosphorylation and inhibiting NF- κ B-DNA binding activity	[12]
Flavone	Luteonin(5)	HMECs-1	↓PI3K, Akt, mTOR, p70S6k; ↓MMP-2, MMP-9, HSP90	Blocking Gas6/Axl pathway and PI3K/Akt/mTOR pathway	[13]
Flavone	Luteonin(5)	Mouse macrophage cells RAW264.7	↓VEGF, HIF-1 α , MMP9	Downregulating HIF-1 α and STAT3 signalling	[14]

Flavone	Luteonin(5)	HUVECs	↓MMP-2, IL-6Rα; ↑SOCS3	Modulating IL-6/STAT3 pathway	[15]
Flavone	Wogonin(6)	Breast cancer MCF-7 cells	↓HIF-1α, VEGF, MMP9; ↑PHD 1, 2, 3 and VHL; ↓EGFR, Cdk4, survivin	Degrading HIF-1α protein	[16]
Flavone	Wogonin(6)	RPMI-8226 multiple myeloma cells	↓VEGF, PDGF, bFGF, VHL complex, VHL sumoylation and ubiquitination, c-Myc, HIF-1α	Modulating c-Myc/HIF-1α/VEGF signaling axis	[17]
Flavone	Wogonin(6)	Human gastric carcinoma in nude mice; HUVECs	↓ ERK1/2, AKT and p38	Inhibiting VEGFR2 phosphorylation	[18]
Flavone	Wogonin(6)	HUVECs	↓VEGF; PI3K and phosphorylation of Akt; ↑PTEN; ↓phosphorylation of IKK and IκB	Suppressing PI3K/Akt/NF-κB signaling	[19]
Flavone	Wogonoside(7)	Breast cancer MCF-7 cells	↓VEGF, Wnt3a; ↑GSK-3β, AXIN; promoting phosphorylation of β-catenin	Suppressing Wnt/β-catenin pathway	[20]
Flavone	Nobiletin(8)	HUVECs	↓ERK1/2, JNK, c-Jun, STAT3, proMMP-2, MMP-2, PA, Upa; ↑caspas3	Inhibiting VEGF- and bFGF-induced signaling and activating caspase pathway	[21]
Flavone	Nobiletin(8)	Human ovarian cancer OVCAR-3 and CP70 cells	↓VEGF, HIF-1α, AKT, NF-κB	Inhibiting Akt phosphorylation	[22]
Flavone	Nobiletin(8)	Breast cancer MCF-7 and T47D cells	↓VEGF, EGFR, bFGF, Src, FAK, STAT3, PXN; MMP2, MMP3, MMP9	Mediating Src/FAK/STAT3 signaling	[23]
Flavone	Oroxylin A(9)	HUVECs	↓phosphorylation of p38 MAPK, ERK1/2, Akt	Blocking KDR/Flk-1 phosphorylation	[24]
Flavone	Oroxyloside(10)	EA.hy926 human endothelial cell-like cell, NSCLC A549 cells	↓phosphorylated VEGFR2, Akt, p38, ERK, IKK, IκB, p65; ↑R-Ras, E-cadherin	Inhibiting Akt/MAPK/NF-κB pathway	[25]
Flavone	Baicalein(11)	NSCLC H-460, A549 and SKMES1 cells, xenografts	↓FGFR-2, VEGF, MMP1, TEK and ANGPT1	Partly mediated via VEGF and FGFR-2 signalling	[26]
Flavone	Baicalein(11)	HUVECs	↓MMP-2; inhibiting migration, proliferation	Reducing cell-associated MMP-2 activity	[27]

			and capillary formation of vascular endothelial cells		
Flavone	Baicalein(11)	Ovarian cancer OVCAR-3 and CP-70 cells	↓VEGF, c-Myc, HIF- α , NF- κ B	Inhibiting VEGF, HIF-1 α , cMyc and NF κ B	[28]
Flavone	Baicalein(11)	BV2 murine microglial cells	↓HIF-1 α , iNOS, COX-2, VEGF	Inhibiting ROS and PI 3K/Akt pathway	[29]
Flavone	Baicalein(11)	HUVECs	↓phosphorylation of VEGF2 and ERK, cyclin D, cyclin E, cdk-4, cdk-6, Rb; ↑p16, p21, p27 and p53	Regulating p53/Rb signaling; inhibiting ERK1/2 and p38 MAPK phospho- activation	[30]
Flavone	Baicalein(11)	HUVECs	↓AKT, ERK1/2, p38, TRAF6	Regulating TRAF6 mediated TLR4 pathway	[31]
Flavone	Genkwanin(12)	HUVECs	↓VEGF-induced invasion, tube formation	Inhibiting invasion and tube formation	[32]
Flavone	Acacetin(13)	Human ovarian cancer OVCAR-3 and A2780 cells	↓HIF-1 α , VEGF and p-Akt	Inhibiting AKT/HIF-1 α pathway	[33]
Flavone	Acacetin(13)	HUVECs	↓VEGF, eNOS, iNOS, MMP-2, bFGF	Suppressing the STAT-VEGF axis	[34]
Flavone	Apigenin(14)	HUVECs	↓E-cadherin, PECAM-1; ↑cleaved caspase-3, PARP, lamin A/C	Blocking the ERK signaling and ERK 1/2 survival signaling	[35]
Flavone	Apigenin(14)	Human ovarian cancer OVCAR-3 and A2780/CP70 cells	↓VEGF, HIF-1 α , HDM2; ↑p53	Regulating PI3K/AKT/p70S6K1 and HDM2/p53 pathways	[36]
Flavone	Apigenin(14)	Human pancreatic cancer S2-013 and CD18 cells	↓HIF-1 α , GLUT-1, VEGF	Downregulating HIF-1 α , GLUT-1 and VEGF	[37]
Flavone	Apigenin(14)	TRAMP mice	↓VEGF, uPA, MMP-2, MMP-9; ↑p-Akt and p-ERK1/2	Attenuating IGF-I/IGFBP-3 signaling	[38]
Flavone	Eupafolin(15)	Hepatocellular carcinoma cell lines HepG2 and Hep3B, HUVECs	↓Phosphorylation of ERK1/2, Akt and VEGF	Blocking VEGFR2 activation, and ERK1/2 and Akt phosphorylation	[39]
Flavone	HMM(16)	Standard reaction buffer	↓Cathepsins B and L	Inhibiting cathepsins B and L	[40]
Flavone	Eupatorin(17)	Human breast cancer MCF-7 and MDA-MB-231 cells	↓Bcl2L11, VEGFA, HIF1A genes; ↑Bax gene	Blocking the phospho-Akt pathway and cell cycle	[41]
Flavone	Sotetsuflavone	NSCLC A549 cells	↓VEGF, HIF-1 α , MMP-9,	Modulating PI3K/AKT and	[42]

	(18)		MMP-13,TNF- α ; \uparrow angiostatin	TNF- α /NF- κ B pathways	
Flavone	Sotetsuflavone (18)	NSCLC A549 cells	\downarrow TGF- β , β -catenin; ZO-1	STAT3, \uparrow endostatin, Inhibiting TGF- β , STAT3 and β -catenin; increasing endostatin and ZO-1	[43]
Flavone	Morusin(19)	Human HCC HepG2 and Hep3B cells, HUVECs	\downarrow Bcl-2, VEGF, MMP2, MMP9, VEGFR2, IL-6 and phosphorylated STAT3; \uparrow Bax, active caspase-3	Attenuating IL-6/STAT3 signaling	[44]
Flavone	Morusin(19)	NSCLC A549 cells	\downarrow Genes expression of VEGF and COX-2	Inhibiting VEGF and COX-2 genes	[45]
Isoflavone	Genistein(20)	Human prostate cancer PC-3 cells, HUVECs	\downarrow VEGF, HIF-1 α	Suppressing autocrine and paracrine signalings	[46]
Isoflavone	Genistein(20)	Human pancreatic carcinoma Capan-1, Capan-2, AsPc-1, PANC-1, and Mia PaCa-2 cells	\downarrow VEGF, HIF-1	Inhibiting hypoxic activation of HIF-1 to downregulating VEGF gene expression	[47]
Isoflavone	Genistein(20)	HUVECs	\downarrow MMP-1, MT1-MMP, pro-MMP-2, TIMP-1, TIMP-2, uPA, PAI-1	Preventing MMP-1 and uPA and the activation of pro-MMP-2, and modulating TIMP-1 and -2, and PAI-1	[48]
Isoflavone	Genistein(20)	Human bladder cancer RT4, T24, TSGH8301 cells	\downarrow VEGF, PDGF-A, TF, uPA, MMP-2, MMP-9; \uparrow PAI-1, endostatin, angiostatin, TSP-1	Inhibiting VEGF, PDGF-A, TF, uPA, MMP-2 and MMP-9; upregulating PAI-1, endostatin, angiostatin and TSP-1	[49]
Isoflavone	Genistein(20)	Human prostate cancer PC3 cells	\downarrow MMP-9, type IV collagenase, uPA, uPAR, protease M, PAR-2, VEGF, VEGFR, TGF-b, BPGF,LPA, TSP; \uparrow CTGF, CTAP	Downregulating type IV collagenase, uPA, uPAR,protease M, PAR-2, VEGF, VEGFR, TGF-b, BPGF,LPA, and TSP, and up-regulating CTGF and CTAP	[50]
Isoflavone	Genistein(20)	HUVECs	\downarrow MMP-2, MMP-9, JNK, p38, PTK	Downregulating JNK and p38 activation	[51]
Flavonol	Quercetin(21)	HUVECs, human prostate cancer PC3 cells	\downarrow mTOR, Akt, p70S6K,	Regulating AKT/mTOR/P70S6K signaling	[52]
Flavonol	Quercetin(21)	Human oral cancer SAS cells	\downarrow MMP-2, MMP-9	Inhibiting NF- κ B and MMP-2/MMP-9 signaling	[53]
Flavonol	Quercetin(21)	Mammary carcinoma model	\downarrow MVD, VEGF, Bfgf, H-ras protein	Inhibiting the H-ras protein synthesis, and VEGF and bFGF	[54]
Flavonol	Quercetin(21)	HUVECs, human	\uparrow TSP-1	Upregulating TSP-1	[55]

		prostate cancer PC3 cells			
Flavonol	Quercetin(21)	Lung cancer squamous carcinoma NCI-H157 cells	↓VEGF, p-Akt, p-STAT3	Suppressing STAT3 tyrosine phosphorylation, and Akt phosphorylation,	[56]
Flavonol	Quercetin(21)	Nasopharyngeal carcinoma NPC039 cells	↓VEGF, NF-κB	Suppressing NF-κB activity	[57]
Flavonol	Quercetin(21)	Bovine aortic endothelial cells	↓eNOS	Suppressing eNOS and early M-phase cell cycle arrest	[58]
Flavonol	Quercetin(21)	Human breast cancer MDA-MB-231 and MCF7 cells, HUVECs	↓COX-2 and PGE2 by inhibiting the binding of the transactivators CREB2, c-Jun, C/EBPβ, NF-κB	Inhibiting the p300 signaling and blocking the binding of multiple transactivators to COX-2 promoter	[59]
Flavonol	QODG(22)	HUVECs	↓VEGFR2, c-Src, FAK, ERK, AKT, mTOR, p70S6K	Suppressing VEGFR2-mediated signaling	[60]
Flavonol	Silibinin(23)	Human bladder transitional cell papilloma RT4 cells	↓Survivin; ↑p53	Downregulating survivin and increase p53	[61]
Flavonol	Silibinin(23)	Colon cancer LoVo cells	↓VEGF; ↑VEGFR1	Upregulating VEGFR-1	[62]
Flavonol	Silibinin(23)	Human prostate DU145 tumor xenografts	↓MVD, VEGF; ↑IGFBP-3	Inhibiting VEGF and endothelial cell growth, and inducing apoptosis	[63]
Flavonol	Silibinin(23)	Female SKH-1 hairless mice	↓HIF-1α, STAT3, NF-κB, COX-2, iNOS, Tyr ⁷⁰⁵ and Ser ⁵³⁶	Inhibiting NF-κB signaling	[64]
Flavonol	Silibinin(23)	Transgenic mouse model of prostate cancer	↓VEGF, VEGFR2, bFGF	Downregulating VEGF, VEGFR-2, and bFGF	[65]
Flavonol	Silibinin(23)	Human colorectal carcinoma HT29 xenograft tumor	↓NOS, NOS3, COX-1, COX-2, HIF-1α and VEGF	Downregulating NOS, COX, HIF-1α, and VEGF expression	[66]
Flavonol	Silibinin(23)	HUVECs	↓MMP-2, survivin; ↑Kip1/p27, Cip1/p21, p53	Downregulating survivin; inhibiting Akt and NF-κB signaling, and MMP-2 secretion	[67]
Flavonol	Silibinin(23)	Human cervical (HeLa) and hepatoma (Hep3B) cells	↓HIF-1α, VEGF	Inhibiting PI3K/Akt signaling	[68]
Flavonol	Silibinin(23)	Human breast cancer MCF-7 cells	↓MMP-9, VEGF	Inactivating the Raf/MEK/ERK pathway	[69]

Flavonol	Myricetin(24)	SKH-1 hairless mouse skin tumorigenesis model	↓HIF-1 α , MMP-9, MMP-13	Suppressing PI-3 kinase activity and attenuating Akt/p70S6K phosphorylation	[70]
Flavonol	Myricetin(24)	Ovarian cancer A2780/CP70 and OVCAR-3 cells	↓VEGF, p-Akt, p-70S6K, HIF-1 α	Modulating Akt/p70S6K/HIF-1 α /VEGF pathway and p21/HIF-1 α /VEGF	[71]
Flavonol	Myricetin(24)	HUVECs	↓Cell migration, tube formation	Suppressing PI3K/Akt/mTOR signaling	[72]
Flavonol	Kaempferol(25)	Ovarian cancer OVCAR-3 and A2780/CP70 cells	↓VEGF, ERK phosphorelation, NF- κ B, cMyc; ↑p21	Regulating ERK-NF- κ B-cMyc-p21-VEGF pathway	[73]
Flavonol	Kaempferol(25)	Ovarian cancer OVCAR-3 and A2780/CP70 cells	↓VEGF, HIF-1 α	Modulating Akt/HIF and ESRR α pathways	[74]
Flavonol	Kaempferol(25)	HUVECs	↓VEGFR2, p-Akt, p-p38	Inhibiting VEGFR2 expression, and VEGF and FGF pathways	[75]
Flavonol	Kaempferol(25)	HUVECs	↓VEGFR2, PI3K, AKT, mTOR, MEK1/2, ERK1/2	Targeting VEGFR2 and downregulating the PI3K/AKT, MEK and ERK pathways	[76]
Flavonol	Kaempferol(25)	HUVECs	↓HIF-1 α , VEGFR2, ERK, p38, Akt, mTOR	Modulating ERK/p38 MAPK and PI3K/Akt/mTOR pathways	[77]
Flavonol	Rhamnazin(26)	HUVECs, human breast cancer MDA-MB-231 cells	↓VEGFR2, MAPK, AKT, STAT3; ↑PEDF	Regulating VEGF and PEDF; downregulating the VEGFR2/STAT3/MAPK/Akt pathway	[78,79]
Flavonol	Galangin(27)	HUVECs	↓VEGF	Downregulating CD44 and VEGF	[80]
Flavonol	Galangin(27)	Ovarian cancer A2780/CP70 and OVCAR-3 cells	↓VEGF, p-Akt, p-70S6K, HIF-1 α	Modulating Akt/p70S6K/HIF-1 α /VEGF pathway	[71]
Flavonol	Fisetin(28)	HUVECs, HT-1080 cells	↓MMP-14, MMP-1, MMP-3, MMP-7, MMP-9	Inhibiting the relational MMPs	[81]
Flavonol	Fisetin(28)	Colorectal cancer	↓MMP-8, MMP-13	Inhibiting MMP-8 and MMP-13	[82]
Flavonol	Fisetin(28)	HUVECs, prostate carcinoma DU145 and lung carcinoma A549 cells	↓Cyclin D1, survivin, VEGF, eNOS, iNOS, MMP-1, -3, -7, -9 and -14, Bcl-2; ↑caspases-3 and caspases-7, PARP, p53, p21, Bax	G1 phrase-G2/M arrest; Downregulating cyclin D1, survivin, VEGF, eNOS, iNOS, MMPs, Bcl-2; inducing p53 and p21, Bax expression and cleavage of caspases-3 and -7, and PARP	[83-84]
Flavonol	Fisetin(28)	Breast cancer 4T1 and JC cells	↓HO-1, MMP-2, MMP-9	Regulated by HO-1 through transcription factor Nrf2	[85]
Flavonol	Fisetin(28)	Human prostate cancer PC-3 cells	↓MMP-2, MMP-9	Inactivating PI3K/Akt and JNK pathways and diminishing NF- κ B and AP-1 DNA-binding activities	[86]

Flavonol	Fisetin(28)	Human cervical adenocarcinoma SiHa and CaSki cells	↓uPA, p-p38, NF-κB	Inhibiting p38 MAPK-dependent NF-κB pathway	[87]
Flavonol	Fisetin(28)	Pancreatic cancer cells	↓NF-κB, MMP9, EGFR, HER-2	Inhibiting DR3-mediated NF-κB activation	[88- 89]
Flavonol	Fisetin(28)	Prostate cancer	↓NF-κB, MAPK, Wnt, Akt, mTOR	Inhibiting NF-κB, MAPK, Wnt, Akt and mTOR	[90-91]
Flavanonol	EGCG(29)	HUVECs	↓VEGFR-2, VEGF;	Inhibiting VEGF-induced VEGFR2 signaling	[92- 93]
Flavanonol	EGCG(29)	Human endothelial cells	↓VEGF, VEGFR-1 and -2, ERK-1 and -2, MMP-2, MMP -9	Downregulating VEGF, VEGFR-1 and -2, ERK-1 and -2, MMP-2 and -9	[94-95]
Flavanonol	EGCG(29)	SW620 colon cancer cells	↓MMP-9, NF-κB p-ERK1/2	Suppressing NF-κB and ERK1/2 signaling	[96]
Flavanonol	EGCG(29)	NSCLC A549 cells	↓VEGF; ↑Endostatin	Increasing endostatin and suppressing VEGF	[97]
Flavanonol	EGCG(29)	Colorectal cancer cells SW837	↓VEGF, HIF-1α, IGF-1, IGF-2, EGF, heregulin mRNAs, VEGFR2, p-VEGFR2, p-IGF-1 receptor, p-ERK, p-Akt	Suppressing HIF-1 and VEGF/VEGFR axis activation	[98]
Flavanonol	EGCG(29)	NSCLC A549 and NCI-H460 cells	↓HIF-1α, VEGF, IL-8, CD31 and Akt	Inhibiting VEGF, IL-8, and CD31 and Akt activation	[99]
Flavanonol	EGCG(29)	Human gastric cancer AGS cells	↓VEGF, p-STAT3	Inhibiting VEGF via suppressing STAT3 activity	[100]
Flavanonol	EGCG(29)	Human gastric cancer SGC-7901 cells	↓VEGF, p-STAT3	Inhibiting the VEGF secretion and STAT3activation	[101]
Flavanonol	EGCG(29)	NSCLC A549 cells	↓ HIF-1α, VEGF, COX-2, p-Akt, p-ERK, vimentin protein, p53, β-catenin	Inhibiting angiogenesis and downregulating HIF-1α and VEGF	[102]
Flavanonol	EGCG(29)	Human prostate carcinoma LNCaP cells	↓VEGF, uPA, angiopoietin 1 and 2, MMP-2 and -9; ↑TIMP1	Downregulating VEGF, uPA, angiopoietin 1 and 2, MMP-2 and -9 and elevating TIMP1	[103]
Flavanonol	EGCG(29)	HUVECs	↓VEGF, endoglin, pSmad1	Downregulating endoglin/pSmad1 signaling	[104]
Flavanonol	EGCG(29)	Human cervical tumour cells (HeLa)	↓TNFAIP2, EFNA1, PDGFA, CXCL6, THBS-1, TGF-β2, CCL2; ↑ANGPTL4, ID1, IFN-β1, IL-1β	Modulating the genes transcription involved in the angiogenic process	[105]
Flavanonol	EGCG(29)	Endothelial cells, endothelial progenitor cells, bone marrow stromal cells	↓ MMP-9, p-Akt; suppressing the CD133 ⁺ /VEGFR2 ⁺ cells into peripheral	Inhibiting Akt phosphorylation and VEGF-induced migration; downregulating MMP-9	[106]

			circulation		
Flavanon ol	EGCG(29)	HUVECs	↓ VEGF-induced DNA synthesis, VEGFR-1 and -2, ERK1/2, EGR1	Inhibiting DNA synthesis and cell proliferation and the signal transduction pathways	[107]
Flavanon ol	EGCG(29)	Mouse breast cancer E0771 cells	↓VEGF, HIF-1 α , NF- κ B	Inhibiting HIF-1 α , NF- κ B and VEGF	[108]
Flavanon ol	EGCG(29)	NSCLC A549 cells	↓HIF-1 α , VEGF	Downregulating HIF-1 α and VEGF	[109]
Flavanon ol	EGCG(29)	HUVECs	↓ MT1-MMP	Inhibiting MT1-MMP to block the endothelial cell invasion	[110]
Flavanon ol	EGCG(29)	Human neuroblastoma SK-N-BE and human fibrosarcoma HT1080 cells	↓MMP-2, MMP-9	Inhibiting MMP-2 and MMP-9	[111]
Flavanon ol	EGCG(29)	Human endometrial cancer cells AN3CA and RL95-2, stromal cells	↓VEGFA, HIF-1 α , CXCL12	Inhibiting PI3K/AKT/mTOR/HIF1 α pathway and downregulating CXCL12	[112]
Flavanon es	Naringenin(30)	Human endothelial cells	↓ICAM-1, IL-6, MCP-1, VEGF, ERR α , KDR, p-Akt, p-paxillin	Mediating ERR α /VEGF/KDR signaling	[113]
Flavanon es	HLBT-001(31)	Ex vivo rat aortic ring	↓ capillary sprout and tube formation	Not mentioned	[114]
Flavanon es	Hesperetin(32)	HUVECs	↓p-PI3K, p-Akt, ERK, JNK, p38	Modulating PI3K/AKT, ERK and p38 MAPK signaling	[115]
Flavanon es	Hesperetin(32)	Rat colon carcinogenesis	↓VEGF, bFGF, EGF and COX-2	Inhibiting angiogenic growth factors and COX-2 mRNA expression	[116]
Flavanon es	Didymin(33)	HUVECs	↓ROS, NF- κ B, and VCAM-1, ICAM-1, E-selectin	Preventing NF- κ B and expression of adhesion molecules	[117]
Flavanon es	Farrerol(34)	HUVECs, HMECs-1	↓p-ERK, p-Akt, p-mTOR, p-JAK2, p-STAT3, Bcl2, Bcl-xl	Downregulating Akt/mTOR, Erk and Jak2/Stat3 signals	[118]
Chalcon e	HSYA(35)	Human gastric adenocarcinoma BGC-823 cells	↓ MVD, IOD	Inhibiting tumor vascularization	[119-120]
Chalcon e	HSYA(35)	Human gastric adenocarcinoma BGC-823 cells	↓VEGF, MMP-9, bFGF, MMP-9 mRNA	Downregulating VEGF, bFGF and MMP-9	[121]
Chalcon e	HSYA(35)	Murine hepatoma H22 cells	↓CD105, VEGFA, bFGF, VEGFR1, p-c-raf, p-ERK1/2, NF- κ B, cyclinD1, c-myc, c-Fos	Blocking ERK/MAPK and NF- κ B signaling	[122]

Chalcone	HSYA(35)	Murine hepatoma H22 cells and HepG2 human hepatocellular carcinoma cells	↓MMP-2, MMP-9, p-p38, ATF-2, COX-2	Inhibiting p38 MAPK phosphorylation	[123]
Chalcone	FLA-16(36)	C6 and U87 gliomas	↓20-HETE, VEGF, HIF-1 α , TGF- β ; ↑survival	Modulating PI3K/Akt signaling through inhibition of CYP4A	[124]
Chalcone	SKLB-M8(37)	HUVECs, B16F10 cells	↓p-ERK1/2	Decreasing ERK1/2 phosphorylation	[125]
Chalcone	LicA(38)	HUVECs	↓VEGFR2, IL-6, IL-8, cSrc	Blocking VEGF/VEGFR-2 signaling	[126]
Chalcone	LicE(39)	4T1 Mammary carcinoma cells	↓VEGFR2, VEGF-A, HIF-1 α , COX-2, iNOS	Decreasing VEGFR2, VEGF-A, HIF-1 α , COX-2, iNOS	[127]
Chalcone	FKB(40)	Two breast cancer cell MCF-7 and MDA-MB231	↓Angiogenin, F3, SDF-1, serpin F1, TSP-2	Reducing angiogenin, F3, SDF-1, serpin F1, and TSP-2	[128]
Chalcone	FKB(40)	MDA-MB231 cells, HUVECs	↓MMP9, VEGF, GLUT1, FOXM1	Suppressing the formation of vessels	[129]
Chalcone	FKA(41)	MDA-MB231 cells	↓VEGF, GLUT1, ICAM1	Inhibiting new blood vessels	[130]
		Bladder tumor tissues in UPII-SV40T transgenic mouse	↓Androgen receptor	Downregulating the androgen receptor	[131]
Chalcone	Cardamonin(42)	SKOV3 cells	↓HIF-1 α , HIF-2 α , VEGF, S6K1	Inhibiting HIF- α and VEGF	[132]
Chalcone	Cardamonin(42)	HUVECs	↓p-ERK1/2, p-AKT	Regulating ERK1/2 and AKT signaling	[133]
Chalcone	Cardamonin(42)	HUVECs	↓miR-21	Downregulating miR-21	[134]
Chalcone	Isoliquiritigenin(43)	HUVECs	↓MMP-2, 1-MMP, JNK, p38 MAPK; ↑TIMP	Hampering MAPK signaling of JNK and p38	[135]
Chalcone	Isoliquiritigenin(43)	HUVECs, MCF-7 and MDA-MB-231cells	↓VEGF, HIF-1 α , VEGFR-2, p-ERK1/2, p-Akt, p-JNK, eNOS, MMP-2	Inhibiting VEGF/VEGFR2 pathway	[136]
Chalcone	Isoliquiritigenin(43)	Adenoid cystic carcinoma cells ACC-M and ACC-2	↓MVD, VEGF, p-mTOR, p-S6, p-ERK1/2; ↑JNK, p-TSC-2	Dual activation of JNK and inhibition of ERK	[137]
Chalcone	Isoliquiritigenin(43)	HUVECs	↓p-ERK1/2, VEGF; ↑PEDF	Inhibiting ERK1/2 and VEGF, and promoting PEDFexpression	[138-139]
Chalcone	TSAHC(44)	TM4SF5-null SNU449Cp or TM4SF5-expressing SNU449Tp stable cells	↓TM4SF5-mediated EMT, multilayer growth, migration, invasion and tumor formation ; p ^{Y577} FAK, p27 ^{Kip1}	Disturbing protein-protein interaction between TM4SF5 and other membrane receptors	[140]
Chalcone	Xanthohumol(45)	HUVECs, SMC	↓NF- κ B	Mitigating NF- κ B activity	[141]

e	45)				
Chalcone	Xanthohumol(45)	MCF7 cells, endothelial cells	↓NF-κB, IL1β	Modulating NF-κB signalling	[142]
Chalcone	Xanthohumol(45)	HUVECs	↑p-AMPK CAMMKβ, LKB1; ↓eNOS, p-mTOR, p-70S6K, p-4EBP1	Inhibiting AMPK and AKT/mTOR pathway	[143]
Chalcone	Xanthohumol(45)	U937 cells, HUVECs	↓VEGF, MMP-2, MMP-9, p-p65, p-cytosolic IκBα, p-Akt	Inhibiting Akt/NF-κB signaling to decrease VEGF secretion	[144-145]
Chalcone	Xanthohumol(45)	KBM-5 cells	↓ICAM-1, MMP-9, VEGF	Inhibiting ICAM-1, MMP-9, and VEGF	[146]
Chalcone	Xanthohumol(45)	BxPC-3 and AsPC-1 cells	↓VEGF, IL-8, NF-κB	Suppressing NF-κB activity	[147]
Chalcone	Xanthoangelol(46)	HUVECs	↓VEGF	Inhibiting tube formation and the binding of VEGF to vascularendothelial cells	[148]
Chalcone	Butein(47)	EPCs	↓p-Akt, p-mTOR, p70S6K, 4E-BP1, eIF4E	Targeting the AKT/mTOR translation dependent signaling	[149]
Chalcone	Butein(47)	Human prostate cancer PC3 and DU145 cells	↓VEGF, MMP-9	Inhibiting NF-κB signaling	[150]

Note: "↓" indicates an increase in indicators; "↑" indicates a decrease in indicators.

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