**Table S2.** Animal studies conducted with dietary phenolics and(or) phenolic-rich extracts on BC models.

| Animal Model (female) | Extract/Compound assayed | Dose/Duration | Main Outcomes | References |
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| **Anthocyanins** | | | | |
| Sprague-Dawley rats; DMBA-induced BC | Concord grape juice concentrate | Diluted in drinking water 1:2, 1:1, and 2:1 (phenolic level 346, 519, and 642 mg/dL, respectively); 19 weeks. | ↓Tumour volume and multiplicity (only at 519 mg/dL); ↓tumour weight (at 346 and 519 mg/dL); ↓DMBA-DNA adducts formation; ↑hepatic GST and catalase; ↓XO. | [1] |
| Wistar-Furth rats; MT-450 xenograft | Delphinidin | Exp. 1: $1.18 \times 10^{-5}$ mol (s.c. injection); 21 days<br>Exp. 2: $1.18 \times 10^{-5}$ mol (p.o.); 28 days. | Results in Exp. 1: ↑tumour growth, lymph node weight and lung metastasis; ↓CD31 and LYVE-1.<br>Results in Exp. 2: ↑tumour growth, lymph node weight and lung metastasis. | [2] |
| Sprague-Dawley rats; NMU-induced BC | Delphinidin | 100 mg/kg/day (diet); 18 weeks. | ↓Tumour incidence; ↓Ki-67 (in pulmonary metastatic tumour tissue and BC tissue). ↓*HOTAIR* expression and ↑miR-34a (in normal and BC tissue). | [3] |
| Immunodeficient BALB/c nude mice; MDA-MB-453 xenograft | Anthocyanin-rich extract from black rice (in the presence or absence of VEGF) | 100 mg/kg/day (p.o.); 28 days. | ↓Tumour growth, proliferation and microvascular density; ↓MMP-2, MMP-9, and urokinase-type plasminogen activator protein level. | [4] |
| BALB/c nude (*nu*/*nu*) mice; MDA-MB-453 xenograft | Anthocyanin-rich extract from black rice | 150 mg/kg/day (p.o.); 21 days. | ↓Tumour growth, pulmonary metastasis, lung tumour nodes and Ki-67. | [5] |
| BALB/c nude mice; MDA-MB-231-Luc-GFP xenograft | Delphinidin-3-glycoside | 40mg/kg/day (p.o.); 28 days. | ↓Tumour growth, *HOTAIR* expression and p-Akt protein level; ↑IRF-1 protein level. | [6] |
| Crl:NU-*Foxn1*$^{nu}$; MDA-MB-231 xenograft | Cyanidin-3-glycoside | 1.6 and 3.2 g/kg (p.o., daily two times); 25 days. | ↓Tumour growth (dose-dependent effect). | [7] |
| **Flavanones** | | | | |

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| Sprague-Dawley rats; DMBA-induced BC | Orange juice<br>Grapefruit juice<br>Naringin<br>Naringenin | Orange and grapefruit juices were administered *ad libitum*, whereas naringin and naringenin were administered at 500 and 240 mg/100 gr diet, respectively (diets containing 5% and 20% corn oil); 15 weeks. | ↓Tumour weight and burden; ↑tumour latency (only naringin and orange juice containing 5% corn oil). ↑Tumour weight (only grapefruit juice containing 20% corn oil). ↓Tumour burden (only naringenin containing 20% corn oil). | [8] |
| Sprague-Dawley rats; DMBA-induced BC | Hesperidin | 30 mg/kg b.w.; 45 days. | Attenuation of the DMBA-induced deregulation on carbohydrate metabolizing enzymes[1], lipid profile[2] (plasma and liver) and ATPases[3] (erythrocytes and liver). | [9] |
| Wistar rats; DMBA-induced BC | Naringenin-tamoxifen (TAM) and Naringenin-TAM-Self-nanoemulsifying drug delivery systems (SNEEDS) | 20 mg/kg; 30 days (60 days for survival assay). | The main effects were exerted by Naringenin-TAM-SNEEDS: ↓tumour growth and burden; ↑survival rate. | [10] |
| Sprague-Dawley rats; DMBA-induced BC | NSD containing [4]Heperetin-Mannitol (MAN)-sodium lauryl sulfate (SLS)-dioctyl sodium sulphosuccinate-DOSS.<br>PM containing [4]Heperetin-MAN-SLS-DOSS.<br>PM containing MAN-SLS-DOSS (placebo). | 20 mg/kg orally (with respect to hesperetin) for each assay; once daily for 106 days. | Effects of NSD and PM treatments: ↑tumour latency; ↓tumour volume and weight; hepatotoxicity attenuation. | [11] |
| Wistar rats; DMBA-induced BC | Naringenin | 2.5, 5, and 10 mg/kg b.w.; 19 weeks. | ↓Tumour incidence, growth and weight; ↓proliferation; ↑apoptosis, caspase-3 and -9; ↑Phase I and II enzymes and ATPases[3] activity. Hepatotoxicity attenuation; modulation carbohydrate metabolizing enzymes[1], antioxidant status[5], mitochondrial mediated-apoptosis markers[6], lipid profile[2], and glycoprotein levels. | [12] |

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| BALB/c mice (4T1 xenograft) and C57BL/6 mice | Naringenin | 100 mg/kg/day (p.o.); up to 35 days (160 days for survival assay). | ↑Survival rate; ↓lung metastases; ↑T cells activation and INF-γ and IL-2 expressing T cells. | [13] |
| BALB/c athymic mice (ovariectomized); MCF-7aro[7] xenograft (and androstenedione) | Hesperetin | 500, 1000 and 5000 ppm; up 13 weeks. | ↓Tumour volume and weight; ↓17 β-oestradiol level in plasma; ↓*pS2* and *CYP1A1* mRNA expression; ↓cyclin D1, CDK4, and Bcl-xL protein level; ↑$p57^{Kip2}$ protein level. | [14] |
| BALB/c athymic mice (ovariectomized); [8]MCF-7aro xenograft (and androstenedione) | Hesperetin (alone or together with letrozole) | 5000 ppm; 84 days. | ↓Tumour volume and weight; ↓17 β-oestradiol level in plasma. Prevention of letrozole side-effects regarding bone deterioration. | [15] |
| BALB/c athymic mice; 4T1/RFP or 4T1/TGF-β1 | Naringenin | 200 mg/kg; 30 days. | Amelioration of the tumour-mediated immuno-supressive environment; ↓pulmonary metastasis; ↓TGF-β1 level in serum and lungs; ↑survival rate. | [16] |
| Obese C57BL/6J mice (ovariectomized); E0771 xenograft | Naringenin | 1 and 3% (w/w) diet; 33 days. | ↓Tumour growth; ↑p-Akt/Akt (T308 and S473) and p-mTOR/m-TOR (S2448) (mainly at 3% in mammary tumor). ↓adipose mass, adipocyte size and *α-SMA*, *MCP-1*, *IL-6*, and *leptin* mRNA expression (in mammary adipose tissue, mainly at 3%). | [17] |
| Athymic nude mice (*nu*/*nu*); MCF-7 or SKBR3 xenograft | 2-Hydroxyflavanone | 25 mg/kg b.w.; p.o. every other day for 8 weeks. | ↓Tumour weight; ↓RLIP76, Ki-67, CD31, p-Akt, surviving, and vimentin; ↓Bcl-2/Bax ratio; ↑E-cadherin | [18] |
| NOD scid gamma mice; TMD231-luc cells | 2-Hydroxyflavanone (alone or together with RLIP antibody + RLIP antisense) | 50 mg/kg b.w.; p.o. every other day for 51 days. | ↓Tumour growth and lung metastasis; ↓RLIP, p-Akt (Ser473) and p-ERK (T202/204); ↓Bcl-2/Bax ratio; ↓Ki-67, CD31, vimentin, CDK4; ↑E-cadherin. | [19] |
| **Flavones** | | | | |

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| Sprague-Dawley rats; BC induced by DMBA and MPA medroxyprogesterone acetate | Apigenin | 0.02, 0.1, and 0.5% (w/w) diet; 56 days. | ↓Tumour incidence (only at 0.1%); ↑tumour multiplicity (at 0.1 and 0.5%). | [20] |
| BALB/c nude mice; MDA-MB-231 xenograft | Apigenin | 25 and 50 mg/kg (in drinking water); 2 weeks. | ↓Tumour growth; ↓pSTAT3/STAT3, pERK/ERK, IL-6, PI3K and p-Akt, N-cadherin. | [21] |
| Wistar rats; DMBA-induced BC | Luteolin (alone or together with cyclophosphamide) | 30 mg/kg (p.o.); 20 days. | ↓Tumour incidence and volume; ↓lipid peroxide formation; ↑SOD, catalase, and GPx level and activity. | [22] |
| BALB/c and athymic nude mice; 4T1 and MCF-7 xenograft, respectivley | Luteolin (alone or together with DOX) | 100 mg/kg (p.o.); 3 weeks. | ↓Tumour growth; ↑survival rate; ↓MDA in serum and ↑MDA in tumour (after luteolin + DOX treatment). ↑SOD, catalase; ↓MDA in plasma and ↑MDA in tumour (after luteolin treatment). | [23] |
| Athymic nude mice; MDA-MB-231 xenograft | Luteolin | 0.01 and 0.05% (w/w) diet; 13 weeks. | ↓Tumour growth and proliferating cells. | [24] |
| Athymic mice (ovariectomized); MCF-7aro$^{7}$ xenograft (and androstenedione) | Luteolin (alone or together with letrozole) | 5, 20, and 50 mg/kg (b.w.); 84 days. | ↓Tumour growth; ↓17β-oestradiol (at 50 mg/kg and together with letrozole); ↓uterine weight; ↑Bax/Bcl-xL; ↑HDL level (at 50 mg/kg); ↓cyclin A, D1, E, CDK4, CDK2, and p57. | [25] |
| BALB/c nude mice; MDA-MB-231 xenograft | Baicalein | 50 and 100 mg/kg (p.o.); 15 days. | ↓Lung and liver metastases; ↓SATB1, Wnt1, vimentin, β-catenin, SNAIL; ↑E-cadherin. | [26] |
| BALB/c nude mice; MCF-7 or MDA-MB-231 xenograft | Baicalein | 100 mg/kg (p.o.); 21 days. | ↓Tumour growth; ↓p-Akt; ↑Bax and LC3 protein level. | [27] |
| BALB/c nude mice; T47D and MDA-MB-231 xenograft | Wogonin | 0.1, 1, and 10 mg/kg (p.o. 6 days per week); 4 weeks. | ↓Tumour growth. | [28] |
| BALB/c nude mice; MDA-MB-231 xenograft | Wogonoside | 80 mg/kg (p.o. once every other day); 21 days | ↓Tumour growth and metastases; ↓MMP-9, vimentin, and twist1; ↑E-cadherin; ↓TNF-γ, TRAF2, and TRAF4. | [29] |

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| BALB/c nude mice; MDA-MB-231 xenograft | Wogonoside | 80 mg/kg (p.o. once every other day); 10 – 15 days. | ↓Tumour growth and angiogenesis; ↓CD31 expression; ↓hemoglobin. | [30] |
| **Flavonols** | | | | |
| Sprague-Dawley rats; DMBA-induced BC | Quercetin (Quer) | 1% (w/w) diet; 51 weeks. | No effects. | [31] |
| Sprague-Dawley rats; DMBA- and NMU-induced BC | Quer | 2% and 5% (w/w) diet; 20 weeks. | ↓Tumour multiplicity, latency and incidence. | [32] |
| Sprague-Dawley rats; DMBA-induced BC | Quer (alone or together with diallyl sulfide) | 10 g/kg diet; 24 weeks. | ↓Cumulative number of tumours (only significant in the presence of diallyl sulfide). | [33] |
| Sprague-Dawley rats; DMBA-induced BC | Quer | 10 or 20 g/kg diet; 107 days. | ↑Tumour latency (only at 20 g/kg). | [34] |
| ACI rats; 17β-oestradiol-induced tumour | Quer | 2.5 g/kg; 8 months. | No protection against 17β-oestradiol-induced tumour; ↓tumour latency; ↓COMT activity. | [35] |
| Wistar rats; DMBA-induced BC | Quer | 50, 100, and 200 mg/kg b.w. (p.o.); 16 weeks. | ↑SOD, GPx, and catalase activity in erythrocyte lysates, plasma and breast tissue; ↓TBARS in plasma and ↑ in breast tissue. | [36] |
| Sprague-Dawley rats; DMBA-induced BC | TAM + Quer and TAM-Quer-NPs | TAM + Quer 3 mg/kg + 6 mg/kg (1:2 w/w), TAM-Quer-NPs equivalent to 3 mg/kg TAM (p.o. in a repeated dose of once in 3 days); 30 days (up to 60 days for survival study). | ↓Tumour growth; ↑survival rate (after TAM-Quer treatment). ↑Quer plasma level; ↓tumour growth; ↑survival rate; ↓MMP-2 and MMP-9 plasma level; ↓hepatotoxicity (after TAM-Quer-NPs treatment). | [37] |
| Sprague-Dawley rats; DMBA-induced BC | Quer and Quer-SNEDDS | 50 and 100 mg/kg; 12 weeks. | ↑Tumour latency; ↓MMP-2 and MMP-9 plasma level; ↓tumour burden; ↓hepatotoxicity (Quer-SNEDDS treatment was the most effective). | [38] |
| Sprague-Dawley rats; DMBA-induced BC | TAM + Quer and TAM-Quer-SNEDDS | TAM + Quer 3 mg/kg + 6 mg/kg (1:2 w/w), TAM-Quer-SNEDDS equivalent to 3 mg/kg TAM (p.o. in a repeated dose of once in 3 days); 30 days (up to 60 days for survival study). | ↑Survival rate; ↓tumour growth and burden; ↓MMP-2 and MMP-9 plasma level; ↓hepatotoxicity (TAM-quer- | [39] |

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| | | | SNEDDS treatment was the most effective). | |
| Wistar rats; DMBA-induced BC | Quer | 100 mg/kg b.w.; 30 days. | Induction of tumour regression; ↓tumour volume; ↓cellular infiltration in breast tissue; Preservation of normal breast tissue architecture; ↑SOD, catalase, and GPx activity; ↓AFP, CA 15-3, and CEA; ↓Hsp70 protein level. | [40] |
| Sprague-Dawley rats; DMBA-induced BC | Quer-RSV-GEN and Quer-RSV-GEN SNEDDS | Quer-RSV-GEN (equivalent to 50 mg/kg/week of Quer) and Quer-RSV-GEN SNEDDS (equivalent to 50 mg/kg/week of Quer); 91 days. | ↑Survival rate; ↓tumour incidence and growth; ↓MMP-2, MMP-9, IL-6 and TNF-$\alpha$ plasma level (Quer-RSV-GEN SNEDDS treatment was the most active). | [41] |
| Sprague-Dawley rats; NMU-induced BC | Rutin (with DOX) | 50 mg/kg (p.o. 7 days per week for 50 days). | ↓Tumour growth in the presence of DOX; ↓side-effects exerted by DOX regarding cognitive function, inflammation, oxidative stress, as well as blood and immune cells. | [42] |
| Athymic *nu/nu* mice; GFP-MDA-MB-231 xenograft | Quer + RSV + Cath | 0.5, 5, and 25 mg/kg (b.w.) each (p.o., 3 times per week); 117 days. | ↓Tumour growth (at 5 and 25 g/kg). | [43] |
| BALB\c and athymic nude mice; 4T1 xenograft | Quer (alone or together with DOX) | 100 mg/kg; 4 – 6 weeks (up to 100 days for survival study). | The effects were mainly observed in BALB\c mice: ↓tumour growth and lung metastases; ↑survival rate; ↑INF-$\gamma$ and IL-2 level; ↓IL-4 and IL-10 level; ↓apoptosis of CD4+ and CD8+ T cells; ↑CD8+ T cells cytotoxicity against 4T1 cells. | [44] |
| Pathogen-free BALB\c mice; 4T1 xenograft | Quer (alone or together with DOX) | 100 mg/kg (p.o.); 3 weeks. | ↓Tumour growth, lung metastases and metastastic tumour weight; ↑ survival rate. Abrogation of the DOX-induced toxicity and modulation of HIF-1$\alpha$ and VEGF expression (only Quer treatment). | [45] |

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| BALB/c and SCDI mice; JIMT-1 xenograft | Quer, vincristine, vincristine + Quer (molar ratio 2:1) and co-encapsulated liposomal vincristine[8]+ Quer (molar ratio 2:1) | Quer (0.24 mg/kg), vincristine (1.33 mg/kg), vincristine + Quer (0.24 mg/kg + 1.33 mg/kg), and co-encapsulated liposomal vincristine + Quer (0.24 mg/kg + 1.33 mg/kg); 60 days. | ↑Circulation time and release *in vivo*; ↓tumour regression; ↑tumour latency and survival rate (co-encapsulated liposomal vincristine + Quer was the most effective treatment). | [46] |
| C3(1)/SV40 Tag | Quer | 0.02, 0.2, and 2% (w/w) diet; 16 weeks. | Dissimilar effects on tumour number: ↑ at 2%, whereas ↓ at 0.2%; ↓tumour volume (dose-dependent); modulation of genes expression related to BC. | [47] |
| Swiss albino mice; Ehrlich ascites carcinoma cells injection | Quer | 1 mg/kg; 50 days (up to 250 days for survival assay). | ↓Tumour growth and Ki-67 level; ↑survival rate; ↑p53 and p-p53 protein level; ↑apoptosis. | [48] |
| BALB/c nude mice; MCF-7 xenograft | Quer | 34 mg/kg; 21 days. | ↓Tumour volume and weight; ↑tumour necrosis; ↓number of oncocytes; ↓microvessel density in tumour; ↓Ki-67 and vWF level; ↓VEGF, VEGF-R2, and NFATc3 (protein and mRNA); ↓calcineurin activity. | [49] |
| BALB/c nude mice; MCF-7 xenograft | Quer and vanadium-Quer complex | Quer (100 mg/kg) and vanadium-Quer complex (20 and 45 mg/kg); 24 weeks. | Preservation of normal breast tissue architecture; ↓cell proliferation; ↑p53; ↑Bax/Bcl2 ratio; ↑apoptosis. | [50] |
| Wistar rats; DMBA-induced BC | Myricetin | 50, 100, and 200 mg/kg; 120 days. | ↓TBARS (plasma and breast tissue); ↑SOD (erythrocyte lysate and breast tissue). | [51] |
| | | **Isoflavones** | | |
| Sprague-Dawley rats; DMBA-induced BC | GEN | 25 or 250 mg/kg diet. GD 0 (*In utero*) to PND 21 (weaning). | ↓Number of tumours; ↓number of TEB and TD; ↓number of lobules type I. | [52] |
| Sprague-Dawley rats; DMBA-induced BC | SPI | 30, 40, and 810 mg/kg diet; from PND 36 to the end of the study (PND 127). | No significant chemopreventive effects. | [53] |
| F-344 rats; NMU-induced BC | SP and IDSP | 10 and 20% for each treatment (w/w) diet; 19 weeks. | No significant chemopreventive effects. | [54] |
| Sprague-Dawley rats; DMBA-induced BC | SPI | Total isoflavones: 430 mg/kg diet (276 mg GEN/kg and 132 mg DAZ/kg diet); lifetime exposure (from GD 0 and for 2 generations). | ↓Tumour incidence (%). | [55] |

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| Sprague-Dawley rats; DMBA-induced BC | SOYSELECT™ extract (12% isoflavones) | 0.35 or 0.7% extract (w/w); from weaning (PND 21) to the end of the study (PND 218). | ↑Degree of tumour differentiation; ↓percentage of ERα and PR positive tumour. | [56] |
| Sprague-Dawley rats; DMBA-induced BC | GEN, DAZ, GEN + DAZ, SPI and SPId | GEN or DAZ (200 mg/kg diet), GEN + DAZ (100 + 100 mg/kg diet), SPI or SPId (160 g/kg diet); from PND 43 to PND 170. | ↓Tumour multiplicity (only DAZ, SPI, and SPId). | [57] |
| Sprague-Dawley rats; DMBA-induced BC | SPI | 430 mg total isoflavones/kg diet (including 276 mg/kg GEN and 132 mg/kg DAZ equivalents); from GD 4 to PND 48. | ↓Hepatic EROD and MROD; ↓mammary CYP1A1, CYP1A2, CYP1B1 (mRNA and protein); ↓AhR and ARNT protein level (although the mRNA was increased). | [58] |
| Sprague-Dawley rats; DMBA-induced BC | SPI | 20% (w/w) diet; from GD 4 (in utero) to the end of the study (PND 21, 33, 50 or between PND 48-51 on metaestrous). | ↓TEB density (not significant); ↑PgR positive cells in TEB. | [59] |
| Sprague-Dawley rats; DMBA-induced BC | GEN | 15, 150, and 300 mg/kg diet; from GD 0 (in utero) to PND 0 (birth). | ↓17β-oestradiol; ↑TEB; ↓lobule (in the offspring at 8 weeks). | [60] |
| Sprague-Dawley rats; DMBA-induced BC | DAZ | 250 mg/kg diet; from PND 0 (birth) to PND 21 (weaning). | No significant chemopreventive effects. | [61] |
| Sprague-Dawley rats (ovariectomized); DMBA-induced BC | GEN | 25 and 250 ppm; 36 weeks. | ↑mean tumour volume (at 25 ppm). | [62] |
| Wistar rats (ovariectomized); | Exp. 1: Soylife, rutin and flaxseed<br>Exp. 2: Novasoy and Soylife<br>Exp. 3: Novasoy and α-oestradiol | Exp. 1: Soylife (0.5%), rutin (0.25%), and flaxseed (10%).<br>Exp. 2: Novasoy (20, 40, and 80 μg/g b.w.) and Soylife (4, 8, 16 μg/g b.w.).<br>Exp. 3: Novasoy (20, 40, and 80 μg/g b.w.) and α-oestradiol (30 μg/g b.w.).<br>90 days. | Exp. 1: ↑*BRCA-1* mRNA expression (only flaxseed).<br>Exp. 2: ↑*BRCA-2* mRNA expression (only at the highest doses). Exp. 3: ↑*BRCA-1* and *BRCA-1* mRNA expression (only at the highest doses). | [63] |
| Sprague-Dawley rats | GEN and SPI$^+$ | GEN (250 mg/kg diet), SPI$^+$ total isoflavones: 394 mg/kg diet (216 and 160 mg/kg diet GEN and DAZ, respectively); from GD 4 (in utero) to PND 50. | ↑Apoptosis in mammary glands; ↑PTEN; ↑*p21*, *Bax*, and *Bok* gene expression (only GEN). | [64] |
| Sprague-Dawley rats; DMBA-induced BC | DAZ and GEN | DAZ (140 mg/kg) and GEN (105 mg/kg (w/w) diet) (both compounds were investigated in the presence or absence of TAM); 114 days. | ↓Tumour multiplicity and incidence; ↑latency; ↓8-OHdG level. | [65] |
| Sprague-Dawley rats; NMU-induced BC | SPI$^+$ diet | Food and water provided *ad libitum* through the study; from GD4 (in utero) to the end of the study (PND165). | ↓Tumour incidence; ↑latency; ↑*HRE2*/*neu* and *PR* gene expression; ↓progesterone in plasma. | [66] |

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| Sprague-Dawley rats; DMBA-induced BC | SP | 20% (w/w) diet; 172 days. | ↓Tumours number and incidence; absence of aggressive grade II and III tumours; ↑tumour latency; ↓angiogenesis; ↓VEGF and bFGF level; ↓proliferation. | [67] |
| Big Blue ® (BB) rats (ovariectomized and normal); DMBA-induced BC | GEN, DAZ and GEN + DAZ | GEN or DAZ (0.25 or 1 mg/kg diet) or GEN + DAZ combined (1 mg/kg diet of each); 23 and 27 weeks. | ↓DMBA-induced mutagenesis (*lac*I and *Hprt*); ↑cell proliferation. | [68] |
| Sprague-Dawley rats; NMU-induced BC | GEN and SPI | GEN (250 mg/kg diet) and SPI diet containing 394 mg isoflavones/kg diet (216 and 160 mg/kg GEN and DAZ, respectively); from GD4 to birth (PND 0) (in utero), and lifetime from GD4 to the final of the study (PND 149). | ↑Tumour latency; ↓tumour multiplicity; ↓higher grade tumour; ↑E-cadherin expression (in utero after SPI treatment). ↑E-cadherin expression (in utero after GEN treatment). ↓Tumour incidence; ↑apoptosis in TEB; ↑PTEN expression; ↑p53 phosphorylation (lifetime after SPI treatment). No effects (lifetime after GEN treatment). | [69] |
| Sprague-Dawley rats; DMBA-induced BC | Soy milk | 0.28 mg/mL isoflavones; 20 weeks. | ↑Mammary tumour incidence and tumour multiplicity. | [70] |
| Sprague-Dawley rats; | Soya and soya + fish oil | Soya (0.5% (w/w) diet (705 mg/kg isoflavonoids)) or soya + fish oil (80 g/kg + 0.5% (w/w)) diet; 14 – 15 days. | ↑TEB; ↑ER-$\alpha$ and ↓ER-$\beta$ (soya diet). ↑Apoptosis (soya + fish diet). | [71] |
| Sprague-Dawley rats (ovariectomized); DMBA-induced BC | GEN, DAZ and SPE | GEN or DAZ (50 mg/kg) diets, and SPE (50 and 100 mg/kg) diet; 20 weeks. | ↓Tumour weight (only after SPE diet); ↓angiogenesis; ↑apoptosis; ↓VEGF level; ↑endostatin level; distinct effect on proliferation: ↑ by GEN and ↓ by SPE. | [72] |
| Sprague-Dawley rats; DMBA-induced BC | IDSP | 3.3 gr/rat/day (dietary administration); 18 weeks (4 weeks before and 14 weeks after DMBA administration). | ↓Tumour growth and incidence; ↑latency; ↓HSP90 and NF-ƙB; ↑p53, p21, and caspase-3; ↑caspase-3 activity; ↓VEGF level. | [73] |
| Wistar rats; DMBA-induced BC | GEN and GEN + lycopene | GEN (2 mg/kg b.w.) and GEN + lycopene (2 + 20 mg/kg b.w.) (p.o. 3 times per week); 20 weeks. | ↓Tumour incidence, growth and development; ↓MDA, 8-isoprostane and 8-OHdG. | [74] |

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| Zucker rats (lean and obese); DMBA-induced BC | SPI | Isoflavones: 3.24 mg/g protein; 22 weeks. | ↑Mammary tumour development (in obese rats); modulation of IGFBP-3 and IGF-1 levels | [75] |
| WKA rats; Ethyl methanesulphonate-induced mammary cancer | GEN and soy diet | GEN (0.03 and 1 mg/g) diet and soy diet (composition not provided); 12 weeks (up to 24 weeks for survival study). | No protective effect of GEN. ↑Latency periods after soy-enriched diet but compared to GEN-treated groups. | [76] |
| Sprague-Dawley rats; PhIP-induced BC | Soymilk (alone or together with $2 \times 10^{11}$ CFU/kg *Lactobacillus casei* Shirota) | 100 g/kg diet (total isoflavones: 335 mg/kg diet). | Effects of soymilk: ↓tumour incidence and multiplicity; ↓body weight (after soymilk treatment). ↓Tumour multiplicity and diameter; ↓body weight and liver relative weight; ↓ER$\alpha$-positive and Ki-67-positive cells; ↓microvessel density (after soymilk + *L. casei*). | [77] |
| Ovariectomized athymic nude mice; MCF-7 xenografts | GEN | 750 ppm; 5 days and 12 weeks. | ↑Tumour growth; ↑uterine and mammary growth; ↑TEB. | [78] |
| Athymic nude mice (ovariectomized); MCF-7 xenografts | GEN and genistin | GEN (750 ppm) and genistin (1200 ppm); from PND 56 to the end of the study (PND 133). | ↑Tumour growth and cell proliferation on MCF-7 tumour; ↑*pS2* gene expression. | [79] |
| Athymic nude mice (ovariectomized); MCF-7 xenografts | SPI and GEN | SPI and GEN diets contain 15, 150, and 300 ppm GEN; 29 weeks. | Dose-dependent effects: ↑tumour growth and cell proliferation on MCF-7 tumour; ↑*pS2* gene expression. | [80] |
| Wild-type (ER$\alpha$WT) and ER-$\alpha$ knockout (ER$\alpha$KO) mice; DMBA-induced BC | GEN | 1 g/kg diet; ~34 weeks. | ↑Malignant tumours (only in ER$\alpha$WT) | [81] |
| Athymic BALB\c mice (ovariectomized); MCF-7 xenografts | GEN | 0.125 – 1 mg/g diet; 22 weeks. | ↑Tumour growth (dose-dependent) and cell proliferation; ↑*pS2* gene expression. | [82] |
| Athymic BALB\c mice (ovariectomized); MCF-7 xenografts | GEN (in the presence of TAM) | 1000 ppm; 32 weeks. | GEN abrogated the effect of TAM: ↑tumour growth; ↑*pS2*, *PR receptor*, and *Cyclin D1* gene expression; ↓17β-oestradiol plasma level. | [83] |

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| MMTV-neu transgenic mice | GEN, DAZ and isoflavone mixture (NovaSoy) | GEN or DAZ (250 mg/kg) diets, and NovaSoy contains 250 mg GEN equivalent/kg diet; from PND 42 to the final of the study (up to 37 weeks). | ↑Tumour latency. | [84] |
| FVB/N-TgN (MMTV-*neu*) mice | Soy diet (Purina 5001) | Isoflavones content: 491 mg/kg (227 mg/kg DAZ and 214 mg/kg GEN); 15 – 60 weeks. | ↑Tumour latency; ↑differentiation of the distal end buds. | [85] |
| Ovariectomized athymic nude mice; MCF-7 xenograft | Soy flour + mixed isoflavones, Molasses, Novasoy®, mixed isoflavones, and genistin | All the diets contained same amount of aglycones GEN equivalents 750 ppm; 11 weeks. | ↑Tumour growth; ↑cell proliferation; ↑*pS2* and *cyclin D1* mRNA expression (after NovaSoy, mixed isoflavones, and genistin treatments). ↑*PgR* mRNA expression (only genistin treatment). | [86] |
| SCDI mice; MCF-7 xenograft | SPC, GSI, BT, GT, SPC + BT, and SPC + GT | SPC (0.1 and 0.5%), GSI (0.014 and 0.028), BT (1.5% (w/v)); GT (1.5% (w/v)); SPC + BT and SPC + GT (0.1% + 1.5% (w/v)); 10 weeks. | ↓Tumour growth (except BT); ↓cell proliferation; ↑apoptosis (BT, GT, and mixtures); ↓vessel density (mixtures); ↓ER-$\alpha$ (BT and mixtures); ↓IGF-I (only SPC + GT). | [87] |
| FVB-Tg.NK (MMTV/c-*neu*) mice (wt-erbB2) | Soy meal, high-dose isolated soy and low-dose isolated-soy | Soy meal contains 491 μg/g isoflavones (214 and 277 μg/g GEN and DAZ, respectively), the high-dose isolated soy contains 491 μg/g isoflavones (214 and 277 μg/g GEN and DAZ, respectively), and the low-dose isolated-soy contains 211 μg/g isoflavones (137 and 74 μg/g GEN and DAZ, respectively); 60 weeks. | ↓Tumour incidence (only soy meal). Low-dose diet blocked the TAM-preventive effects. | [88] |
| FVB-Tg.NK (MMTV/c-*neu*) mice | Isoflavone-concentrate Prevastein | High-fat (20% w/w) diet supplemented with 0.004, 0.02 and 0.06% (w/w) Prevastein; 24 weeks. | ↑Tumour size and multiplicity (at the highest dose). | [89] |
| BALB\c (nude) mice (ovariectomized); MCF-7 xenografts | GEN (in the presence or absence of 17β-oestradiol) | GEN: 500 ppm; 17 weeks. | ↑Tumour growth (in the presence or absence of 17β-oestradiol). ↑Uterine wet weight (in the absence of 17β-oestradiol). | [90] |
| Athymic BALB\c mice (ovariectomized); MCF-7 xenografts | DAZ and equol | 125 – 1000 ppm; 21 and 37 weeks. | ↑MCF-7 tumour growth and *pS2* expression (only DAZ treatment). | [91] |

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| SCID mice; MCF-7 xenografts | GEN and SPC (alone or together with TAM) | GEN (0.07% w/w diet), SPC (0.2 and 0.5% w/w diet); ~80 days. | Effects of GEN: ↓tumour growth; ↓*pS2* and *EGFR* gene expression; ↓proliferation; ↓17β-oestradiol; ↑apoptosis (only with TAM); ↓*ER-α* gene expression; ↓angiogenesis. Effects of SPC: ↓tumour growth; ↑apoptosis; ↓proliferation (alone at 0.5% and with TAM); ↓angiogenesis (only with TAM). | [92] |
| Tg.NK (MMTV/c-*neu*) mice | Isoflavone-concentrate Prevastein | 90 mg/kg mixed in high-fat (24% w/w) diet prepared with corn or fish oil; from 2 weeks before mating to PND 21 (perinatal), from PND21 to the end of the study (postweaning), and from 2 weeks before mating to the end of the study (lifetime). | ↓Tumour incidence and delayed tumour onset. | [93] |
| BALB/c nude mice (ovariectomized); $^{9}$MCF-7Ca xenograft | GEN (in the presence or absence of androstenedione and letrozole) | 250, 500, and 1000 ppm; 19 and 31 weeks. | In absence of androstenedione and letrozole: ↑tumour growth; ↑*pS2* gene expression (at 250 and 500 ppm); ↓*aromatase* gene expression (at 1000 ppm); ↑proliferation. In presence of androstenedione and letrozole: ↑tumour growth (dose-dependent); ↑pS2 (mRNA and protein); ↑17β-oestradiol; ↑aromatase protein level; ↑proliferation; ↑uterine wet weight (dose-dependent). | [94] |
| BRCA-1$^{tm1Cxd}$ heterozygous (+/-) and wild type mice; DMBA-induced BC | GEN | 500 ppm; from PND 15 – PND 30. | Effects on wild type mice: ↓tumour incidence; ↓high-grade tumours; ↑*BRCA1* mRNA expression; ↓CK5 and CK18; ↓TEB and ductal elongation; ↓PR in mammary gland and tumour; ↓ER-α and HER2 in mammary tumour; | [95] |

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| | | | ↓*amphiregulin* and *RankI* gene expression.<br>Effects on BRCA-1$^{+/-}$ mice: ↓CK5 and CK18; ↓TEB and ductal elongation; ↓HER2 in mammary tumour; ↓*amphiregulin* gene expression. | |
| Transgenic MMTV-erbB2 mice | Soybean-enriched diet (20% soybean) | Total isoflavones: 2.6 mg/g diet; from 7 weeks of age to the final of the study (up to 60 weeks). | ↓Breast tumour incidence at high oestrogen level, but ↑breast tumour incidence at low oestrogen level. | [96] |
| MMTV-*Neu* and ERΔ3/*Neu* | Soy diet | Total isoflavones: 619 mg/kg diet (GEN: 191 mg/kg diet, DAZ: 143 mg/kg diet, GLY: 39 mg/kg diet); from 2 months of age to the final of the study. | No effect of soy diet on tumour development; ↑metastatic lesions in ERΔ3/*Neu* mice. | [97] |
| Nu/Nu Nude mice Crl:NU-*Foxn1nu* (MDA-MB-231 xenograft) and C3(1)-SV40 Tag mice | GEN (in the presence or absence of TAM) | 250 mg/kg diet; 5–6 weeks. | Effects on Nu/Nu nude mice Crl:NU-*Foxn1nu*:<br>↓tumour growth (in absence or presence of TAM); ↑ER-$\alpha$ (gene and protein);<br>↓DNMT1 and HDAC1 (gene expression, protein level, and enzymatic activity).<br><br>Effects on C3(1)-SV40:<br>↓tumour growth (in absence or presence of TAM); ↑latency tumour; ↑ER-$\alpha$ (gene and protein); ↓DNMT1 (gene expression and activity); ↓HDAC1 (gene expression, protein level, and activity). | [98] |
| Transgenic Wnt1-Tg mice | SPI | Total isoflavones: 430 mg/kg diet; fom PND 21 (weaning) to the final of the study. | Modulation of epithelial subpopulations in mammary tissue; ↓progesterone; ↓17β-oestradiol; ↓IL-6; modulation of expression of genes related to inflammation, cytokine signaling, and proliferation; | [99] |

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| | | | ↓mammospheres formation in culture; ↓tumour latency and incidence. | |
| MTB-IGFIR transgenic mice (doxycycline supplemented diet) | SPI | Isoflavones: 1660 ppm (daidzin: 463 ppm, DAZ: 95 ppm, genistin: 933 ppm, GEN: 101 ppm, glycetin: 57 ppm, GLY: 9 ppm); from GD 0 (*in utero*) to the final of the study (up to PND 365). | ↑Tumour incidence and onset; ↑ER signaling markers (*Pgr* and *Areg*); ↑CK5 and CK14; ↑p63; ↓lung metastasis. | [100] |
| Germ-free RAG2$^{-/-}$ athymic mice transplanted with breast cancer patients' fecal suspensions obtained before and after chemotherapy treatment (DOX and docetaxel); MDA-MB-231 xenografts | GEN | 250 mg/kg; 8 weeks. | ↓Tumour growth; ↑tumour latency; modulation of gut microbiota at Phylum (i.e., Phylum *Verrucomicrobia*), family (i.e., *Lachnospiraceae* and *Ruminococcaceae*) and genera level (*Lactococcus* and *Eubacterium*). | [101] |
| C3(1)-SV40 Tag transgenic mice | GEN and GEN + broccoli sprouts (BSp) | GEN (250 mg/kg), GEN + BSp (250 mg/kg + 13% (w/w)) diets; from 4 weeks of age to the final of the study. | ↑Tumour latency. | [102] |
| BALB/c mice; 4T1 xenograft | DAZ | 145 mg/kg (p.o.); 20 days of exercise training followed by 22 days of orally administration of DAZ. | Effects of DAZ: ↓tumour growth; ↑Fas, ↑FADD, ↑Bax, ↑Cyt-C, ↑Apaf-1 ↑cleaved caspase-3 and 9, and ↓Bcl-xL. Effects of DAZ + exercise: ↓tumour growth; ↑IL-6 and epinephrine; ↑infiltration of NK cells; ↑apoptosis; ↑Fas, ↑FADD, ↑Bax, ↑Cyt-C, ↑Apaf-1, ↑cleaved caspase-3 and 9, and ↓Bcl-xL. | [103] |
| **Flavan-3-ols/Proanthocyanidins** | | | | |
| Sprague-Dawley rats; DMBA-induced BC | GT Cath | 1% (w/w) diet; PND 56 – PND 294. | ↑Survival rate; ↓tumour size. | [104] |
| F344 rats; PhIP-induced BC | GT Cath | 1% (w/w) diet; up to 52 weeks. | ↓Tumour size | [105] |
| Sprague-Dawley rats; DMBA-induced BC | GT Cath | 0.01, 0.1, or 1% (w/w) diet; 34 weeks. | ↓tumour multiplicity at 0.01 and 1% (lack of dose-dependent effect). | [106] |
| Sprague-Dawley rats; DMBA-induced BC | Black tea | 1.25, 2, and 2.5% (w/v) in water; up to 17 weeks. | ↓Tumour burden and tumour weight per TBA (only 2%). | [107] |
| Sprague-Dawley rats; DMBA-induced BC | GT | 0.3% (w/v) in water; PND 30 – PND 175. | ↓Tumour burden; ↓invasive tumour; ↑latency. | [108] |

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| Sprague-Dawley rats; dual organ tumour model: DMBA-induced BC and azoxymethane-induced colonic aberrant crypt foci formation | Grape seed proanthocyanidins | 0.1, 0.5, and 1% (w/w) diet; 27 weeks. | No effect on mammary tumourigenesis. | [109] |
| F344 rats; PhIP-induced BC | GT Cath | 1% (w/w) diet; 52 weeks. | ↓Tumour size. | [110] |
| Sprague-Dawley rats; DMBA-induced BC | EGCG | 0.065% (w/v) in drinking water; Lifetime: from birth (PND 0) to the end of the study (PND 176). | No effects on mammary tumourigenesis. | [111] |
| Fisher-344 and Sprague-Dawley rats; MNU-induced BC | Polyphenon E | 333 and 1000 mg/kg b.w. (p.o. 7 times per week); 121 days of treatment. | No effects on mammary tumourigenesis. | [112] |
| BALB/c mice; 4T1 cells xenograft | GTP (60% EGCG) | 0.2 and 0.5% (w/v) in drinking water; 36 – 60 days. | ↓Tumour growth; ↓proliferation (PCNA); ↓lung metastasis; ↑survival time; ↑cleaved caspase 3 and Bax/Bcl-2. | [113] |
| C3(1) SV40 *T,t* antigen transgenic multiple mammary adenocarcinoma mice | GT Cath or BT theaflavins | 0.01 or 0.05% (w/v) in water; from 4 weeks of age to the end of the study. | ↑Survival rate; ↓tumour diameter; ↑cleaved caspase-3 level. | [114] |
| Athymic nude mice (NCr-nu/nu); MDA-MB-231 xenograft | GTP and EGCG | GTP (1% (w/v) in drinking water) and EGCG (1mg per animal (p.o. in 100 mL distilled water)); 70 days. | ↓Tumour volume; ↓cell proliferation; ↑apoptosis. | [115] |
| C57BL\6 mice; E0771 xenograft | EGCG | 0.5 g/L in drinking water; 24 days. | ↓Tumour growth and angiogenesis; ↓VEGF level (plasma and tumour). | [116] |
| BALB/c mice; 4T1 cells xenograft | GT extract | 0.6 g/kg (orally fed everyday); 4 weeks. | ↓Tumour weight; ↓lung and liver metastasis; ↓breast cancer-induced bone destruction. | [117] |
| BALB/c mice; 4T1 cells xenograft | EGCG | 0.25, 0.5, 1, and 2 mg/mL in drinking water; 51 days. | ↓Tumour growth (dose-dependent); ↓accumulation of MDSCs in blood, spleen, and tumour; ↑CD4+ and CD8+ T cells. | [118] |
| Nude mice (ovariectomized); MCF-7 xenograft | GTE (alone or in combination with TAM) | 2.5 g/L in water; 64 days. | ↓ER$\alpha$ level; ↓tumour volume and angiogenesis; ↑necrosis and apoptosis (GTE + TAM was the most effective treatment). | [119] |
| Wistar rats; MNU-induced BC | GTE, Epican Forte, Epican Forte + nutrient mix, Epican Forte + Quer and Epican Forte + nutrient mix + Quer | GTE (30 mg), Epican Forte (30 mg), Epican Forte + nutrient mix (130 + 405 mg), Epican Forte + Quer (130 + 0.3 mg), and Epican Forte + nutrient mix + Quer (130 + 405 + 0.3 mg); 60 days. | ↓Tumour volume, weight and multiplicity (Epican forte + nutrient mix + quercetin was the most effective treatment). | [120] |

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| C3H/OuJ mice | GTE (alone or together with TAM) | 0.1 or 1% (w/v) in water; PND 70 – PND 336 weeks. | ↓Tumour incidence (no tumour development in green tea + TAM group); ↓proliferation. | [121] |
| **Stilbenes** | | | | |
| Sprague-Dawley rats; NMU-induced BC | RSV | 10 and 100 mg/kg b.w. (p.o. 5 days/week); 127 days. | RSV at 100 mg/kg: ↓tumour incidence and multiplicity; ↑tumour latency; ↑alveolar and adipocyte differentiation. | [122] |
| Sprague-Dawley rats; DMBA-induced BC | RSV | 100 μg/rat in the diet; 127 days. | ↓Ductal carcinoma induction; ↓tumour incidence and multiplicity; ↑tumour latency; ↓NF-kB activation; ↓COX-2; ↓MMP-9 level. | [123] |
| Sprague-Dawley rats; DMBA-induced BC | RSV | 1 g/kg diet; from PND 0 (birth) to the end of the study (PND ~180). | ↓Number of tumours; ↑tumour latency; ↑differentiated lobular structures; ↓cell proliferation in terminal ductal structures; ↑apoptosis. | [111] |
| Sprague-Dawley rats; DMBA-induced BC | RSV | 100 μg/rat in the diet; 24 weeks. | ↓DNA damage; ↓4-hydroxynonenal level; ↓lipid peroxidation; ↑apoptosis; ↑caspase-3; ↓5-LOX expression; ↓$LTB_4$ formation; ↓NF-kB p65; ↑TGF-β1; ↓cell proliferation. | [124] |
| Sprague-Dawley rats; NMU-induced BC | RSV (alone or in combination with melatonin) | 100 mg/kg diet; 18 weeks. | ↓Tumour incidence; ↓invasive and *in situ* carcinomas. | [125] |
| ACI rats; subcutaneous administration of 17β-oestradiol | RSV | 5 and 25 mg/kg/day; 21 weeks. | ↓*DNMT 3b*; ↓*DNMT1* (only at 25 mg/kg/day); ↑miRNA-21, miRNA-129, miRNA-204, miRNA-489 (in breast tumour tissue). | [126] |
| Sprague-Dawley rats; NMU-induced BC | RSV (alone or in combination with celecoxib) | 100 mg/kg b.w.; 16 weeks. | Effects of RSV + celecoxib: ↓tumour incidence; ↓tumour | [127] |

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| | | | volume; ↓tumour frequency; ↓number of malignant tumours; ↑mammary tumour latency; ↑GDF15 protein expression; ↓*COX-2* gene expression; ↓ROS in lymphocytes. | |
| Sprague-Dawley rats; exposure to TCDD | RSV | 7 ppm; from GD7 to PND 0 (birth). | ↓TD + TEB; ↑ alveolar bud; ↑AhRR protein expression; ↑*BRCA-1* gene expression; ↓*BRCA-1* promoter CpG methylation; ↓*CDK4* gene expression; ↓*Cyclin D1* gene expression; Dissimilar effect regarding *CYP1A1* gene expression: down-regulation at PND 46, and up-regulation at PND 71. | [128] |
| Sprague-Dawley rats; DMBA-induced BC | RSV, RSV-CoenzQ10 SNEDDS, RSV-CoenzQ10-$\alpha$-tocopherol SNEDDS | RSV (50 mg/kg), RSV-CoenzQ10 SNEDDS and RSV-CoenzQ10-$\alpha$-tocopherol SNEDDS (equivalent to 50 mg/kg RSV); 91 days. | ↓Tumour latency and growth; ↓MMP-2 and MMP-9; ↓IL-6 and TNF-$\alpha$; ↑survival rate. RSV-CoenzQ10-$\alpha$-tocopherol SNEDDS was the most effective treatment, what was related to the highest level of RSV and coenzQ10 achieved in plasma. | [129] |
| Wistar rats; NMU-induced BC | RSV | 20 mg/kg b.w.; GD 10 – PND 21. | ↓Number of tumours; ↓tumour weight; ↑apoptosis; modulation of genes related to apoptosis (i.e., *caspase-3* and *Bcl-2*); modulation of morphological changes in mammary tissue (such as ↓ TEB and TD). | [130] |
| Sprague-Dawley rats; NMU-induced BC | RSV | 100 mg/kg b.w. (p.o.); 16 weeks. | ↓Tumour volume, frequency and incidence; ↑latency; ↑number of leukocytes; ↑ROS in leukocytes. | [131] |
| Sprague-Dawley rats; DMBA-induced BC | RSV | 50 mg/kg (p.o., every other day); 18 weeks. | Modulation of oestrogen level (serum and breast tissue). | [132] |

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| FVB/N HER-2/*neu* mice | RSV | 1 mg/L (diluted in water); 11 weeks. | ↓Number and size mammary tumour; ↓lung metastases; ↑apoptosis; HER-2/*neu* down-regulation. | [133] |
| Athymic *nu/nu* mice; GFP-MDA-MB-231 xenografts | RQC | 0.5, 5, and 20 mg/kg b.w. (3 times per week); 117 days. | ↓Tumour area (at 5 and 20 mg/kg b.w.). | [43] |
| Athymic *nu/nu* mice; GFP-MDA-MB-435 xenografts | RQC | 5 mg/kg b.w. (p.o. three times per week); 70 days. | ↓Tumour area and metastasis; modulation of expression of PI3-kinase pathway genes. | [134] |
| Hairless SCDI mice; GFP-MDA-MB-231 xenograft | RQC (alone or together with gefitinib) | (i) 5 mg/kg b.w. each; 84 days. | ↓Tumour growth and metastasis (RQC + gefitinib was the most effective treatment). | [135] |
| Hairless SCID mice (GFP-MDA-MB-231) or athymic nu/nu mice (MDA-MB-435 xenografts) | RSV | 0.5, 5, 50 mg/kg b.w. (p.o. 5 days/week); 44 days (GFP-MDA-MB-435) or 108 days (GFP-MDA-MB-231). | ↑Tumour growth; ↑lung metastasis (only significant at 5 and 50 mg/kg); ↑ Rac activation. | [136] |
| Δ16HER2 mice | RSV | 1 mg/L in water (4 mg RSV/mouse was the daily dose assumed); 15 weeks. | ↓tumour latency; ↑tumour multiplicity; ↑Δ16HER2 expression; ↓ERα expression; inhibition of proteasome activity. | [137] |
| BALB\c homozygous, Crl:NU(NCr)-Foxn1nu; MBCDF-T cells xenograft | RSV (alone or together with calcitriol) | 1.2 g/kg (p.o. 3 times a week); 3 weeks. | ↓Angiogenesis (RSV and calcitriol). | [138] |
| | | **Curcumin** | | |
| Sprague-Dawley rats; DMBA-induced BC | Curcumin | 10 or 20 g/kg diet; 107 days. | ↑Tumour latency (only at 20 g/kg). | [34] |
| Sprague Dawley rats; DMBA-induced BC | Curcumin, Dibenzoylmethane | *Mammary adduct assay:* 0.2 and 1% of both compounds; 10 days. *Tumour inhibition:* curcumin (1% w/w diet) and dibenzoylmethane (0.1, 0.5, and 1% w/w diet); 14 days. | Only dibenzoylmethane: ↓tumour incidence (dose-dependent effect); ↓DMBA-DNA adducts formation (at 1%); ↑liver GST, quinone reductase, and EROD (at 1%). | [139] |
| Sprague Dawley rats; DMBA-induced BC | Turmeric, ethanolic turmeric extract, curcumin-free aqueous turmeric extract | Turmeric (1% w/w diet), ethanolic turmeric extract (0.05% w/w diet), and curcumin-free aqueous extract (1% in water; w/v); 4 weeks (*initiation period)* and 20 weeks (p*ost-initiation period*). | Effects *initiation period*: ↓tumour incidence, burden and multiplicity (turmeric and ethanolic turmeric extract). Effects *post-initiation period*: ↓tumour multiplicity (ethanolic turmeric extract and curcumin-free aqueous turmetic extract). | [140] |

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| Wistar-MS rats; irradiation with γ-rays (gestational period) and subcutaneous implantation of diethylstilbestrol pellet | Curcumin | 1% diet (w/w); 13 months. | ↓Tumour incidence; ↓serum prolactin; ↓TBARS. | [141] |
| Wistar-MS rats; irradiation with γ-rays (gestational period) and subcutaneous implantation of diethylstilbestrol pellet | Curcumin | 1% diet (w/w); GD 11 – PND 0 (birth). | ↓Tumour incidence and latency; ↑LH level. | [142] |
| Athymic *nu/nu* mice; MCF-7 or BT-474 xenograft | Curcumin | 25 gr/kg diet; 3 days. | ↑Tumour growth (in mice treated with cyclophosphamide). | [143] |
| Athymic nude (*nu/nu*) mice; MDA-MB-435LVB xenograft | Curcumin (alone or together with PAX) | 2% diet (w/w); 5 weeks. | ↓BC metastases to the lungs; ↓NF-ƙB activation; ↓COX-2 and MMP-9 levels. | [144] |
| CD-1 Foxn1$^{nu}$ mice; MDA-MB-231 xenograft | Curcumin | 1% diet (w/w); 35 days. | ↓Metastases. | [145] |
| Athymic nude mice; ENU1564 xenograft | Curcumin, meriva | Curcumin (2% w/w diet) and Meriva (6% w/w diet); 20 days. | Effects only in the Meriva-treated group: ↓breast cancer metastases to the lungs; ↓MMP-9 level. | [146] |
| Nude (Foxn1$^{nu/nu}$) mice; MBA-MB-231 xenograft | Curcumin | Curcumin (0.6% w/w diet); 6 weeks. | ↓Tumour growth; ↓NF-kB; ↓PECAM-1; ↓cyclin D1; ↓p65. | [147] |
| CD1 athymic nude mice; MDA-MB-231 xenograft | Curcumin (alone or together with EGCG) | 200 mg/kg/day; 10 weeks. | ↓Tumour volume; ↓EGFR; ↓VEGFR-1; ↓Akt (synergic effects: curcumin and EGCG). | [148] |
| NCr-nu/nu mice; MDA-MB-231 xenograft | Curcumin (alone or together with PAX) | 100 mg/kg; 5 weeks. | ↓Tumour diameter; ↓PCNA-positive cells in tumour; ↑apoptosis; ↑MMP-9. | [149] |
| Swiss albino mice; Ehrlich ascites carcinoma cells xenograft | Curcumin (alone or together with DOX) | 25 and 50 mg/kg b.w. (p.o., every oher day); 21 days. | ↓Number of cancer cells in tumour; ↓DOX-induced toxicity; ↑survival rate. | [150] |
| Swiss albino mice; DMBA-induced BC | Curcumin (alone or together with cyclophosphamide or PAX) | 40 mg/kg b.w. (p.o.); 4 weeks. | ↓Tumour volume; ↓PKC; ↓NF-ƙB; ↓HDAC1 and 2 (curcumin enhanced effects of cyclophosphamide and PAX. | [151] |
| SENCAR (SENsitive to CARcinogen) mice; DMBA-induced BC | Curcumin (alone or together with DHA) | 0.2% diet (w/w); 19 weeks. | ↓Tumour incidence, burden and width (per gram body); ↑tumour differentiation and latency; ↑ER-*α*; ↑maspin protein level; ↓survivin protein level. | [152] |

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| Athymic nu/nu mice; MDA-MB-231 xenograft | Curcumin (alone or together with ABT-888) | 20 mg/kg b.w. (3 times per week); 7 weeks. | ↓Tumour growth. | [153] |
| BALB\c mice; MCF-10A-Tr xenograft | Curcumin (alone or together with RSV) | 20 mg/kg/day (each treatment); 14 days. | ↓Cyclin D1; ↓p21; ↓Gli-1; ↓SHH (27 and 52 kDa); ↓c-Myc (synergic effects between curcumin and RSV). | [154] |
| BALB\c mice; EMT6/P mouse breast carcinoma cells xenograft | Curcumin (alone or together with metformin) | 50 mg/kg (100 μL by oral gavage everyday); 14 days. | ↓Tumour weigh; ↑necrosis; ↑apoptosis; ↑INF-γ and IL-4 (synergic effects between curcumin and metformin). | [155] |
| BALB\c mice; 4T1 xenograft | Curcumin (alone or together with arabinogalactan) | 100 mg/kg/day; 32 days. | ↓Tumour weight and volume; ↓Ki67; ↑p53. | [156] |
| BALB\c and athymic nude mice; BALB-neuT mammary cancer cells xenograft | Curcumin (alone or together with chloroquine) | 2 mg/50 mL maize oil (3 times per week); Up to 35 days. | Effects of curcumin: ↓tumour volume (also in the presence of chloroquine); ↑mice survival; autophagy induction; ↓p62 protein level. | [157] |
| BALB/c nu/nu and athymic nude mice; MDA-MB-231, 4T1, JC, TuBo xenografts | Curcumin SMEDDS | 100 mg/kg (p.o. 100 μL SMEDDS formulation); 1 – 2 months. | ↓Tumour volumen. | [158] |
| BALB/c homozygous, Crl:NU(NCr)-Foxn1nu; MBCDF-T cells xenograft | Curcumin (alone or together with calcitriol) | 40 mg/kg (p.o. every day); 3 weeks. | Effects of curcumin and calcitriol: ↓tumour volume ↓angiogenesis; ↓integrin expression. | [138] |
| Swiss albino mice; Ehrlich ascites carcinoma xenograft | Curcumin (alone or together with PAX or PAX + Vitamin $D_3$) | 50 mg/kg (p.o. 3 times per week); 3 weeks. | ↓Tumour volume and survival rate; ↑necrosis (after curcumin + PAX and Vitamin D3). ↓Tumour volume and survival rate; ↑necrosis; ↑MRD-1 (after curcumin + PAX). | [159] |
| **Lignans/Flavonolignans** | | | | |
| Sprague-Dawley rats; DMBA-induced BC | Flaxseed flour | 5% (w/w) diet; PND 21–21 weeks after DMBA administration (PND 50). | ↓Tumour size. | [160] |
| Sprague-Dawley rats; DMBA-induced BC | Flaxseed flour | 5% (w/w) diet; 25 weeks on the diet. | Modulation of the n-3 and n-6 fatty acids in mammary gland and mammary tumour. | [161] |
| Sprague-Dawley rats; DMBA-induced BC | Sec-Dig, flaxseed oil and flaxseed | Sec-Dig (2.2 μmol/day (p.o. in water)), flaxeed oil (1.82% (w/w) diet), flaxeed (2.5 and 5% (w/w) diet); 7 weeks. | ↓Tumour volume, incidence and number of tumours per rat; modulation of the n-3 and n-6 | [162] |

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| | | | fatty acids in mammary tumour. | |
| Sprague-Dawley rats; MNU-induced BC | Flaxseed and Sec-Dig | Flaxseed (2.5 and 5%) and Sec-Dig dose equivalent to that consumed in 2.5 (Low Sec-Dig) and 5% (High Sec-Dig) flaxseed groups; 22 weeks. | ↓Tumour invasiveness; ↓poorly differentiated tumours. ↓Tumour multiplicity (high Sec-Dig) and ↑tumour multiplicity (low Sec-Dig). | [163] |
| Sprague-Dawley rats; MNU-induced BC | Flaxseed and Sec-Dig | Flaxseed (5% w/w diet) and Sec-Dig (1.5 mg equivalent to that consumed in flaxseed diet); 4 weeks. | ↓IGF-1 level in plasma (effect in the presence or absence of NMU). | [164] |
| Sprague-Dawley rats; DMBA-induced BC | Flaxseed and Sec-Dig | Flaxseed (10% w/w diet) and Sec-Dig (20.1 mg/100 g diet; equivalent to that consumed in flaxseed diet); PND 0 – PND 21 (weaning). | ↓Tumour incidence, burden, number, size, and weight. | [165] |
| Sprague-Dawley rats; DMBA-induced BC | Defatted flax flour | 152 g/kg diet; GD 7 (in utero) – PND 0 (birth). | ↑Apoptosis; ↑*p53* mRNA expression (but not protein). | [166] |
| Sprague-Dawley rats; DMBA-induced BC | Flaxseed | Flaxseed (5 and 10% w/w diet); 2 periods: GD 7 (in utero) – PND 0 (birth) and PND 5 – PND 25. | First period effects: ↑ER-$\alpha$ level (lobular and ductal tissue); ↓ER-$\beta$ level (lobular tissue); ↑tumour multiplicity (at 10%); ↓latency. Second period effects: ↓ER-$\alpha$ level (lobular tissue); ↓ER-$\beta$ level (TEB and lobular tissue); ↑tumour multiplicity and ↓latency (at 10%). | [167] |
| Germ-free Sprague-Dawley rats; DMBA-induced BC | Flaxseed | 5% (w/w) diet; 13 weeks. | ↓Tumour incidence and growth; ↓number of tumours per tumour bearing rat; ↓proliferation; ↑apoptosis; ↑enzyme activity in liver; and plasma: CAT, SOD, and GST (effects in gnotobiotic rats colonized with the lignan-converting bacteria[10] compared to germ-free rats). | [168] |
| Hemiovariectomized ACI rats; DMBA-induced BC | Sec-Dig | 10 and 100 ppm; 3 months. | ↑ESR1; ↑ESR2; ↑CDH2 and ↓*MKi-67* (only at 10 ppm). | [169] |
| TG.NK (MMTV/c-*neu*) transgenic mice | Flaxseed oil and Flaxseed oil + melatonin | Flaxseed oil (0.05, 0.1, and 0.2 mL; made up to 0.2 mL with corn oil) and flaxseed oil + melatonin (0.1 + 100 mg/kg b.w.; made up to 0.2 mL with corn oil); 30 weeks. | ↓Tumour weight; ↓IGF-1 level in plasma; ↓number of tumours per mouse. | [170] |

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| Athymic nude mice (Ncr *nu*/*nu*); MDA-MB-435 xenograft | Flaxseed | 10% (w/w) diet; 8 weeks. | ↓Tumour growth rate; ↓metastasis; ↓Ki-67 ↓IFG-I; ↓EGFR. | [171] |
| Athymic nude mice (Ncr *nu*/*nu*); MDA-MB-435 xenograft | Flaxseed | 10% (w/w) diet; 7 weeks. | ↓Tumour growth rate and metastasis; ↓VEGF. | [172] |
| Ovariectomized athymic mice BALB\c *nu*/*nu*; MCF-7 xenograft | Flaxseed (alone or together with TAM and in the presence of high/low doses of 17β-oestradiol) | Flaxseed (10% w/w diet); 6 and 7 weeks (at high and low doses of 17β-oestradiol, respectively). | ↓Tumour volume, ↓Ki-67 level, and ↑apoptosis (flaxseed alone or together with TAM at 6 weeks); ↓tumour weight (together with TAM at 6 weeks). Attenuation of the ↑tumour volume and weight exerted by TAM at 7 weeks. | [173] |
| Athymic nude mice (Ncr *nu*/*nu*); MDA-MB-435 xenograft | Flaxseed, flaxseed oil, Sec-Dig, flaxseed oil + Sec-Dig | Flaxseed (10% w/w diet), flaxseed oil (36.53 g/kg diet), Sec-Dig (0.2 g/kg diet), flaxseed iol + Sec-Dig (36.53 + 0.2 g/kg diet); 6 weeks. | ↓Metastasis incidence (including lung and lymph nodes). ↓tumour area; ↓apoptosis; ↓Ki-67 level; ↑MDA level in tumour. | [174] |
| Athymic nude mice (Ncr *nu*/*nu*); MDA-MB-435 xenograft | Flaxseed, flaxseed oil, Sec-Dig, flaxseed oil + Sec-Dig | Flaxseed (10% w/w diet), flaxseed oil (36.53 g/kg diet), Sec-Dig (0.2 g/kg diet), flaxseed iol + Sec-Dig (36.53 + 0.2 g/kg diet); 7 weeks. | ↓Metastasis incidence (including lung and lymph nodes). | [175] |
| Ovariectomized athymic mice BALB\c *nu*/*nu*; MCF-7 xenograft | Flaxseed and Flaxseed + SPI | Flaxseed (10% w/w diet) and flaxseed + SPI (10% + 20% w/w diet); 19 weeks. | Flaxseed had no effect on tumour growth but attenuated the stimulating effect of SPI. | [176] |
| Ovariectomized athymic mice BALB\c *nu*/*nu*; MCF-7 xenograft | Flaxseed | 10% (w/w) diet; 5 weeks. | ↓Tumour growth and angiogenesis. ↓extracellular VEGF level. | [177] |
| Ovariectomized athymic mice BALB\c; MCF-7 xenograft | Flaxseed (alone or together with TAM) | 5 and 10% (w/w) diet; 16 weeks. | Flaxseed alone exerted tumour size regression, whereas in the presences of TAM attenuated the stimulating growth effect of TAM; ↓cell proliferation; ↓apoptosis; ↓cyclin D1; ↓HER2; ↓IGF-IR; ↓ER-$\alpha$. | [178] |
| Ovariectomized athymic mice BALB\c *nu*/*nu*; MCF-7 xenograft | Flaxseed (alone or together with TAM) | 5 and 10% (w/w) diet; 8 weeks. | ↓Tumour growth and proliferation; ↑apoptosis; ↑ER-$\alpha$ level; ↓PgR level; ↓IGF-I. | [179] |

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| Ovariectomized athymic mice BALB\c *nu/nu*; MCF-7 xenograft | Flaxseed and Flaxseed + SPI | Flaxseed (10% w/w diet) and flaxseed + SPI (10% + 20% w/w diet); 2 or 25 weeks. | ↓pMAPK level (at 2 weeks). ↑Proliferation; ↑cyclin D1; ↑ER-$\alpha$ level (effects at 25 weeks of flaxseed + SPI) | [180] |
| Athymic nude mice BALB\c; MDA-MB-231 xenograft | Flaxseed and Sec-Dig | Flaxseed (10% (w/w)) diet and Sec-Dig (dose equivalent to that consumed in flaxseed diet); 4 weeks. | ↓Tumour growth. ↑Zn serum level (after flaxseed treatment); ↓Zn serum level (after Sec-Dig treatment); ↑gene expression of the Zn transporter *LIV-1* gene expression. | [181] |
| Ovariectomized athymic mice BALB\c *nu/nu*; MCF-7 xenograft | Flaxseed; Flaxseed hull; Sec-Dig | Flaxseed (10% w/w diet), flaxseed huul (1 g/kg diet), and Sec-Dig (18 g/kg diet); 7 weeks. | Effects of Flaxseed and Sec-Dig: Tumour regression; ↑apoptosis; ↓Bcl-2; ↓cyclin D1; ↓pS2; ↓ER-$\alpha$ and ER-$\beta$; ↓EGFR; ↓IGF-IR; ↓cell proliferation; ↓pMAPK (only Sec-Dig); ↓HER2 (only flaxseed). Effects of Flaxseed hull: ↓cell proliferation; ↑Bcl-2. | [182] |
| Athymic nude mice; MA782, MCF-7, T47D, MDA-MB-435s xenograft | Mix of neolignans isolated from *Vitex Negundo* | 20, 40, and 80 mg/kg (p.o.); 16 or 20 days. | ↓Tumour growth (dose-dependent). | [183] |
| Ovariectomized athymic mice BALB\c *nu/nu*; BT-474 xenograft | Flaxseed oil + trastuzumab | 80 g/kg diet; 4 weeks. | ↓Tumour growth; ↓proliferation; ↑apoptosis. | [184] |
| Ovariectomized athymic mice BALB\c *nu/nu*; MCF-7 xenograft | Flaxseed oil, Sec-Dig or flaxseed oil + Sec-Dig (all the treatments performed in the presence of TAM) | Flaxseed oil (38.5 g/kg diet), Sec-Dig (1 g/kg), and Flaxseed oil + Sec-Dig (38.5 and 1 g/kg diet); 7 weeks. | ↓Tumour growth (only flaxseed oil); ↓proliferation; ↑apoptosis; modulation of ER- and growth factor mediated signaling pathways (mRNA and protein)[11]. | [185] |
| Ovariectomized athymic mice BALB\c *nu/nu*; MCF-7 xenograft | Flaxseed oil, Sec-Dig or flaxseed oil + Sec-Dig | Flaxseed oil (38.5 g/kg diet), Sec-Dig (1 g/kg), and Flaxseed oil + Sec-Dig (38.5 and 1 g/kg diet); 7 weeks. | Tumour regression (in Sec-Dig and flaxseed oil treatments). ↓Tumour growth (only Sec-Dig treatmemt); ↓proliferation; modulation of ER- and growth factor mediated signaling pathways (mRNA and protein)[11]. | [186] |

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| Ovariectomized athymic mice BALB\c *nu/nu*; MCF-7 xenograft | Flaxseed oil | 40 g/kg diet; 8 weeks. | ↓Tumour growth; ↓proliferation; ↑apoptosis; ↓n-6/n-3 PUFA ratio; ↓p-MAPK, Akt and HER2 levels. | [187] |
| Tg.NK (MMTV/*c-neu*) transgenic mice | Flaxseed | 60, 180, or 540 mg/kg diet; 2, 6 or 23 weeks. | ↓Number of tumours per mouse; ↓tumour incidence (at 540 mg/kg diet); ↓GST (at 180 and 540 mg/kg diet); ↑cytochrome P450 enzymes CYP1A1 and 1A2 (at 60 mg/kg diet). | [188] |
| Ovariectomized athymic mice BALB\c *nu/nu*; MCF-7 xenograft | Cotyledon fraction isolated from flaxseed (alone or together with TAM) | 82 g/kg diet; 7 weeks. | Induction of tumour regression; ↓cell proliferation; ↑AIB1 level; ↓HER2 and p-HER2 level; ↓ER$\alpha$ and p-ER$\alpha$ level; ↓*IGF-IR* mRNA expression; ↓*pS2* mRNA expression. | [189] |
| Athymic nude mice BALB\c *nu/nu*; MCF-7 xenograft | Flaxseed and enterolactone | Flaxseed (10% (w/w) diet) and enterolactone (100 mg/kg); ~20 days. | ↓Tumour growth rate and angiogenesis; ↓murine IL-1$\beta$; ↑murine and human IL-1R$\alpha$. | [190] |
| Ovariectomized athymic mice BALB\c *nu/nu*; MCF-7 xenograft | Sec-Dig and sesamin | Sec-Dig (1 g/kg) and sesamin (1 g/kg); 8 weeks. | ↓Proliferation; ↓HER2 and EGFR (Sec-Dig treatment). ↓Tumour growth and proliferation; ↑apoptosis; ↓HER2, EGFR, and p-MAPK (sesamin treatment). | [191] |
| Ovariectomized athymic mice BALB\c *nu/nu*; BT-474 xenograft | Flaxseed (alone or together with trastuzumab) | 10% (w/w) diet; 5 weeks. | Flaxseed + trastuzumab: ↓Tumour growth; ↑survival rate; ↓p-Akt1 protein level; ↓*HER2* mRNA expression ↓n-6/n-3 PUFA ratio. | [192] |
| Ovariectomized athymic mice BALB\c *nu/nu*; BT-474 xenograft | Flaxseed oil (alone or together with trastuzumab) | 4% (w/w) diet; 4 weeks. | Effects of flaxseed oil + trastuzumab: ↓tumour growth and proliferation; ↑apoptosis; ↓*ERBB2, EGFR*, and *MAPK2*; mRNA expression; ↓p-HRE2 protein level; ↓n-6/n-3 PUFA ratio. | [193] |

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| Swiss albino mice; Erhlich ascites carcinoma | Flaxseed, flaxseed meal and flaxseed oil | 10% each treatment; 3 weeks. | ↑Tumour latency; ↓ER level; ↓Ki-67, PgR, IGF, VEGF and MMP-2; ↑caspase-3. | [194] |
| C57BL/6J mice; DMBA-induced BC | Flaxseed oil | 78 g/kg diet; from gestation – PND 21. | ↑Tumour incidence in presence of carcinogen. ↑TEB; accelerated puberty onset; ↑17β-oestradiol level; ↑mammary gland cell proliferation; modulation of cancer-associated KEGG pathways (in absence of carcinogen). | [195] |
| C57BL/6J mice; E0771 xenograft | Sec-Dig | 25, 74, and 100 mg/kg diet; 11 weeks. | Non-tumour bearing mammary glan: ↓Crown-like structures; ↓*ADGRE1* and *Ccl2* mRNA expression. Tumour bearing mammary gland: ↓Tumour growth; ↓*ADGRE1* mRNA expression; ↓p-p65; modulation of NF-ƙB target genes expression. | [196] |
| Sprague-Dawley rats; MNU-induced BC and MMTV-neu-transgenic mice | Silymarin | Rats: 0.03, 0.1, 0.3, and 1% (w/w) diet; PND 21 – PND 161 (140 days). Mice: 0.3% (w/w) diet; PND 28 or 120 – PND ~10 months. | ↑Number of tumours (in rats). ↑Breast tumour incidence and multiplicity (in mice). | [197] |
| FVB/N HER-2/neu transgenic mice | Silybin-phosphatidylcholine complex (IdB 1016) | 450 mg/kg (equivalent to 414 μM/kg silybin); administered daily or twice a week for 1 month. | ↓Tumour incidence, multiplicity and lung metastases; ↓HER/*neu* gene expression; ↑senescence; ↑infiltration of neutrophils, CD4 and CD8 cells. | [198] |
| C3(1) SV40 T,t antigen transgenic multiple mammary adenocarcinoma mouse | Silybin or Silipide | 0.2% (w/w) diet; up to 177 days. | No effects described. | [199] |
| BALB\c and SCDI CB17-Prkdcscid/J mice; 4T1 xenograft | Silybin | 150 mg/kg (p.o., 3 times per week); 4 – 5 weeks. | ↑Survival rate; ↓tumour growth; ↓MDSC accumulation; ↑T-cell accumulation; ↑TNF-α and IL-1β; ↓IL-10 and CCR2 (in BALB\c). No effects described in SCDI mice. | [200] |

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| BALB\c nude mice; MDA-MB-468 | Silybin | 200 mg/kg; 45 days. | ↓Tumour volume; ↓*COX-2*, *MMP-9*, and *VEGF* gene expression; ↓COX-2 and VEGF protein level. | [201] |
| Sprague-Dawley rats; DMBA-induced BC | Silymarin | Basal diet supplemented with 0.5% (w/w) of silymarin nanoparticles; 6 months | ↑8-OHdG; ↑apoptosis; ↓ErbB-2 level in plasma; ↓total antioxidant capacity. | [202] |
| C57BL/6; Ca 755 xenograft | Silybin (free or mixture with lecithin) | 20 mg/kg b.w. (p.o.); 10 days. | ↑Lifespan. | [203] |
| | | **Hydrolysable tannins** | | |
| Sprague-Dawley rats; DMBA-induced BC | EA (alone or together with selenomethionine) | 0.4 g/kg diet; 25 weeks. | ↓Cumulative number of tumours (only significant in the presence of diallyl sulfide). | [204] |
| F344 rats; PhIP-induced BC | EA | 0.1% (w/w) diet; up to 52 weeks. | No significant effects. | [105] |
| F344 rats; PhIP-induced BC | EA | 0.1% (w/w) diet; up to 52 weeks. | No significant effects. | [110] |
| ACI rats; 17β-oestradiol-induced BC | Dehydrated powered blue berry, freeze-dried black raspberry and EA | Dehydrated powered blue berry (1 and 2.5% (w/w) diet); freeze-dried black raspberry (1 and 2.5% (w/w) diet) and EA (400 ppm); up to 26 weeks. | ↓Tumour incidence and multiplicity; ↓*CYP1A1* and *17β-HSD7* expression; ↓COMT (in blue berry treatment). ↓Tumour incidence, growth and incidence; ↑mammary and pituitary weight; ↓*CYP1A1* and *CYP1B1* expression; ↓COMT (in black raspberry treatment). ↓Tumour incidence, volume and multiplicity; ↓*17β-HSD7* expression; ↓COMT (in EA treatment). | [205] |
| ACI rats; 17β-oestradiol-induced BC | EA (alone or together with 17β-oestradiol) | 400 ppm; up to 28 weeks. | Amelioration of the dysregulation induced by 17β-oestradiol on miRNA expression (miR-206, miR-182, miR-375, miR-127, miR-183, miR-122) and their targets at gene and protein level (ER$\alpha$, cyclin D1, RASD1, FoxO3a, FoxO1, cyclin G1, Bcl-w, and Bcl-2). | [206] |

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| Sprague-Dawley rats; DMBA-induced BC | Pom emulsion | 0.2, 1, and 5 g/Kg (p.o. 3 times a week); 18 weeks. | ↓ER-$\alpha$, ER-$\beta$, and ER-$\alpha$/ER-$\beta$; ↓$\beta$-catenin expression and cytoplasmic accumulation; ↓cyclin D1 expression. | [207] |
| Sprague-Dawley rats; DMBA-induced BC | Pom emulsion | 0.2, 1, and 5 g/Kg (p.o. 3 times a week); 18 weeks. | ↓Tumour incidence and weight; ↓proliferation; ↑apoptosis, Bax/Bcl-2 (mRNA and protein), Bad, caspase-3, caspase-7, caspase-9, PARP, and cytochrome-c. | [208] |
| Swiss albino mice; Ehrlich ascites carcinoma cells injection | EA | 3 mg/kg; 50 days. | ↓Tumour growth. | [48] |
| BALB/c athymic nude mice; MDA-MB-231 xenograft | Penta-*O*-galloyl-$\beta$-D-glucose | 20 mg/kg/day b.w. (p.o.); 36 days. | ↓Tumour growth. | [209] |
| BALB/c athymic nude mice; MDA-MB-231 xenograft | Penta-*O*-galloyl-$\beta$-D-glucose | 10 mg/kg/day b.w. (p.o.); 36 days. | ↓Tumour growth and metastasis; ↓Ki-67, CD34, p-STAT, and VEGF level; ↑apoptosis. | [210] |
| BALB/c athymic mice (*nu*/*nu*); MDA-MB-468 | Gallotannin | 0.5% in drinking water (w/v) or daily i.p. injections (10 mg/kg, 5 injections per week); 30 days. | ↓Tumour growth; ↓CcnD1 protein level; ↑p-Chk2. | [211] |
| SCDI mice; MDA-MB-231 luciferase 2 xenograft | EA (alone or together with MRS2179) | 120 μg/mL in drinking water; 16 weeks. | ↓Tumour growth and lung metastasis. | [212] |
| MMTV-PyMT transgenic mice | EA | 50 mg/kg/day (p.o.); 15 weeks. | ↓Tumour growth, burden and lung metastasis; ↑tumour latency and survival rate; ↓cancer stem cells population. | [213] |

[1]Hexokinase, phosphoglucoisomerase, aldolase, glucose-6-phosphate, fructose-1,6-diphosphate, and fructose-6-phosphate; [2]Total, free and ester cholesterol, phospholipids, triglycerides, free fatty acids; [3]$Na^+K^+$-, $Ca^{+2}$-, and $Mg^{+2}$-ATPase; [4]Hesperetin:MAN:SLS:DOSS (2.00:7.74:0.20:0.06); [5]TBARS, GSH, SOD, nitrate, protein carbonyl, catalase, GR, vitamin C and E; [6]Bcl-xL, Bcl-2, Bad, cytochrome C, VDAC, Bax, Apaf-1, and pro-caspase-9; [7]MCF-7aro: MCF-7 breast cancer cells transfected with human CYP19; [8]Vincristine was loaded into ESM/cholesterol/$PEG_{2000}$-ceramide/Quer (72.5:17.5:5:5); [9]MCF-7Ca: aromatase-expressing MCF-7 cells; [10]*Clostridium saccharogumia*, *Eggerthella lenta*, *Blautia producta*, and *Lactonifactor longoviformis*; [11]mRNA: *pS2*, *PgR*, *ERα*, *ERβ*, *CD1*, *EGFR*, *IGF-IR*, *Bcl2*, *HER2*; proteins: ER$\alpha$, HER2, MAPK, AIB1, Akt.

Abbreviations: ADGRE1, adhesion G protein-coupled receptor 1; AFP, alpha-pheto protein; AIB1, amplified in breast 1; AhRR, aromatic hydrocarbon receptor repressor; $\alpha$-SMA, alpha smooth muscle actin; Bad, Bcl-2 associated agonist of cell death; BC, breast cancer; bFGF, basic fibrobast growth factor; BRCA1, Breast Cancer Type 1 susceptibility protein; BT, black tea; b.w., body weight; CA 15-3, breast cancer specific marker; Cath, catechin; CCR2, C-C chemokine receptor type 2; CEA, carcinoembryonic antigen; CK, cytokeratin; CoenzQ10, co-enzyme Q10; COMT, cathecol-*O*-methyltransferase; COX-2, cyclooxygenase-2; DAZ, Daidzein; DHA, docosahexahenoic acid; DMBA, 7,12-dimethylbenz[$\alpha$]antracen; DNMT, DNA methyltransferase; DOX, doxorubicin; EA, ellagic acid; EGCG, epigallocatechin gallate; EGFR, epithelial growth factor receptor; ER, oestrogen receptor; ER$\alpha$, oestrogen receptor alpha; ER$\beta$, oestrogen receptor beta; EROD, Ethoxyresorfurin-*O*-deethylase; ESM, egg sphingomyelin; EXM, exemestrane; Exp., experiment; FoxO, Forkhead box; GD, gestation day; GEN, genistein; Gli-1, Zinc finger protein; GLY, glycetein; GPx, glutathione peroxidase; GSI, genistin-rich soy isoflavone mixture; GST, glutathione S-transferase; GT,

green tea; GTE, greent tea extract; 17β-HSD7, 17β-dehydrogenase 7; HER2, human epidermal growth factor receptor 2; HDAC: histone deacetylase; 8-OHdG, 8-hydroxy-2'-deoxyguanoside; HOTAIR, HOX transcript antisense RNA; IDSP, isoflavone-depleted soy protein; IGF-1, insulin-like growth factor 1; IGF-IR, insulin-like growth factor receptor; IPSP, isoflavone-poor soy protein; IRF-1, interferon regulatory factor 1; LH, luteinizing hormone; LTB4, leukotriene B4; LYVE-1, lymphatic vessel endothelial hyaluronan receptor 1; MDA, malondialdehyde; MDSC, myeloid-derived suppressor cells; MMP, metalloproteinase; MPA, medroxyprogesterone acetate; MROD, methoxyresorufin-*O*-demethylase; NMU, N-nitroso-N-methylurea; NPs, nanoparticles; NSD, Nanocrystalline solid dispersions; PARP, poly(ADP) ribose polymerase; PAX, paclitaxel; PCNA, proliferating cell nuclear antigen; PECAM-1, platelet endothelial adhesion molecule 1; PEG2000, polyglycerol stearate; pERα, phospho-oestrogen receptor alpha; PgR, progesterone receptor; PhIP, 2-amino-1-methyl-6-phenylimidazo[4,5-b]pyridine; PKC, protein kinase C; PM, physical mixture; pMAPK, phospho-specific mitogen-activated protein kinase; PND, postnatal day; Pom, pomegranate; pS2, marker for hormone-dependent breast cancer; p.o., *per os* (oral administration); PTEN, phosphatase and tensin homolog; PUFA, polyunsaturated fatty acid; Quer, quercetin; RASD1, RAS dexamethasone-induced 1; RQC, RSV + Quer + Cath; s.c., subcutaneous; RSV, resveratrol; Sec-Dig, secoisolariciresinol diglycoside; SCID, Severe Combined Immune-Deficient; SMEDDS, self-microemulsifying drug delivery system; SNEDDS, self-nanoemulsifying drug delivery system; SP, soy protein; SPC, soy phytochemical concentrate; SPE, soy phytochemical extraction; SPI, soy protein isolate; SPId, soy protein isolate depleted of isoflavones; SSH, sonic hedgehog; SOD, superoxide dismutase; TAM, tamoxifen; TBARS, thiobarbituric acid reactive substances; TCDD, 2,3,7,8-tetrachlorodibenzo-p-dioxin; TD, terminal duct; TEB, terminal end bud; TGF-β1, transforming growth factor-β1; TNF-α, tumour necrosis factor alpha; TRAF, TNF receptor associated factors; VEGF, vascular endothelial growth factor; XO, xanthine oxidase.

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