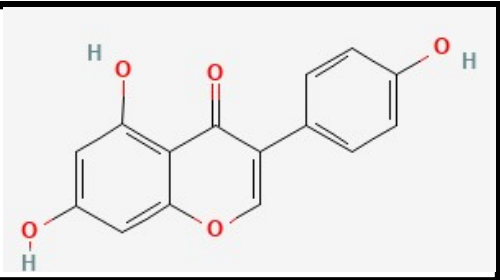
purobest
HIGH PURITY • BEST QUALITY

GENISTEIN

COMMON NAME: Soy
CHEMICAL CLASS: Isoflavones
SCIENTIFIC NAME: 5,7-Dihydroxy-3-(4-hydroxyphenyl)-4H-1-benzopyran-4-one



CLINICAL PROPERTIES

- Anti-inflammatory activity (1)
- Antioxidant activity (1), (2)
- Antibacterial and Anti-diabetic activity (3), (2)
- Anticancer activity (4), (5)
- Neuroprotective activity (6)

CLINICAL APPLICATIONS IN ONCOLOGY

- Genistein selectively affects genes in the prostate of humans that regulate cancer cell motility and metastasis. (13)
- The inhibition of the prostaglandin pathway may contribute to the beneficial effect of soy isoflavones in PCa chemoprevention and/or treatment. (15)
- Genistein could be safely added to chemotherapy. (4), (5)

CLINICAL SAFETY AND TOXICITY

Oral formulations of genistein were well-tolerated up to doses of 8 mg/kg in cancer patients with no serious side effects. Only mild side effects like a treatment-related rash, blood pressure and neutrophil count reduction at 16 mg/kg , elevations in lipoprotein lipase and hypophosphatemia at 8 mg/kg were observed. (7), (8), (9)

MECHANISM OF ACTION

1) Induction of apoptosis. (19), (20), (21), (22), (23), (24), (25)
2) Regulation of Cancer-associated Micro RNA's. (33), (34–36), (37), (38), (39), (40)
3) Anti metastatic Effect. (22), (29)
4) Anti-proliferative effect. (41), (42), (43), (44), (45), (46), (47), (48)
5) Anti angiogenic Effect. (30), (31), (32)
6) Cell Cycle Arrest. (19), (26), (21), (27), (28)

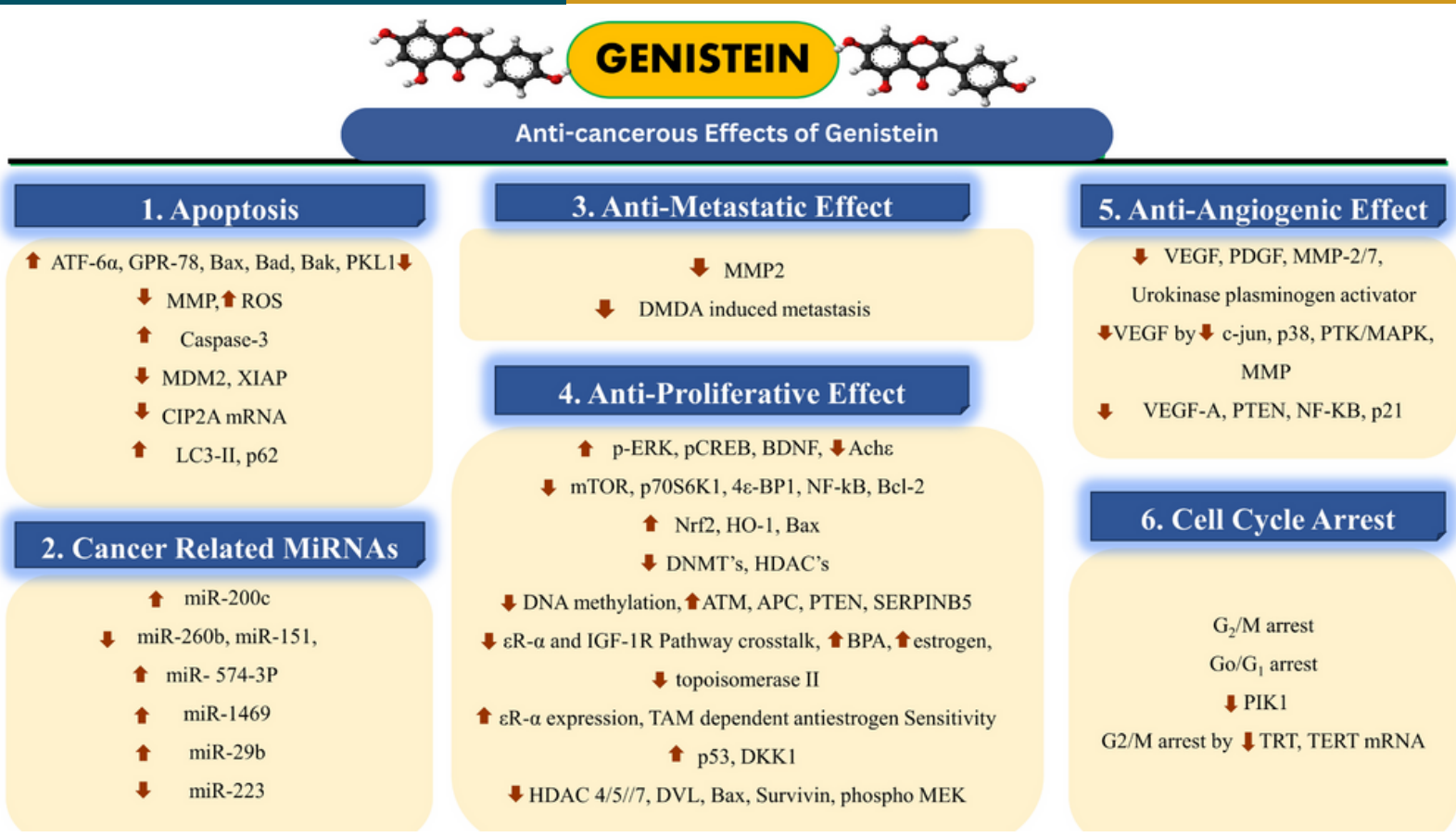


FIGURE A. The effect of Genistein on multiple targets to exert antitumor effect

GENISTEIN AND BREAST CANCER

In breast cancer, genistein is involved in multiple pathways related to:

Cell Cycle Arrest

- Activates G2/M phase arrest and the ATM/Cdc25C/Chk2/Cdc2 checkpoint pathway. (47)
- Increase interaction among integrins, FAK, and CDC42. (35)
- Inhibits GPR30. (48)

Apoptosis

- Reduces Cu(II) to Cu(I) through reactive oxygen species (ROS). (49)
- Increases caspase 3,7 and 12 to induce apoptosis. (50)
- Decrease EGFR and HER2. (51)
- Downregulates mir-155, which upregulates FOXO3a, p27, and PTEN expression. (52)
- Increases Sirt1 gene. (42)
- Prevents TNF-α-induced NF-κB translocation in nucleus, and ↓IL-1β. (53)
- Degrades proto-oncogene c-Fos and prohibits protein 1 (AP-1) and ERK expression. (54)
- Downregulates p90RSK. (55)
- Increases Ca2+-dependent pro-apoptotic protease, mμ-calpain. (50)
- Downregulates NCOA2 and NCOA3. (56)
- Downregulates Hedgehog signaling. (52)

Proliferation Inhibition

- Reduces Fis1 and Opa1 mRNA expression. (52)
- Reduces P-STAT3/STAT-5. (57)
- Downregulates mRNA expression of ER-α protein. (58)

Metastasis Inhibition

- Inactivates Protein Tyrosine Kinase which reduces MMP-2,7. (59)
- Downregulates ATP synthase/ cytochrome c oxidase ratio. (52)

Chemosensitivity

- Activates ER-β receptor and increases chemotherapeutic efficacy. (60)

Angiogenesis Inhibition

- Blocks the transactivation of downstream HIF-1α effectors, i.e. VEGF. (61)
- Downregulates COX-2. (62)
- Targets the Receptor Tyrosine Kinases and ↓IGF-1R. (52)

Inhibition of mammosphere formation

- Suppresses PI3K/Akt signaling by upregulating the PTEN expression. (63)

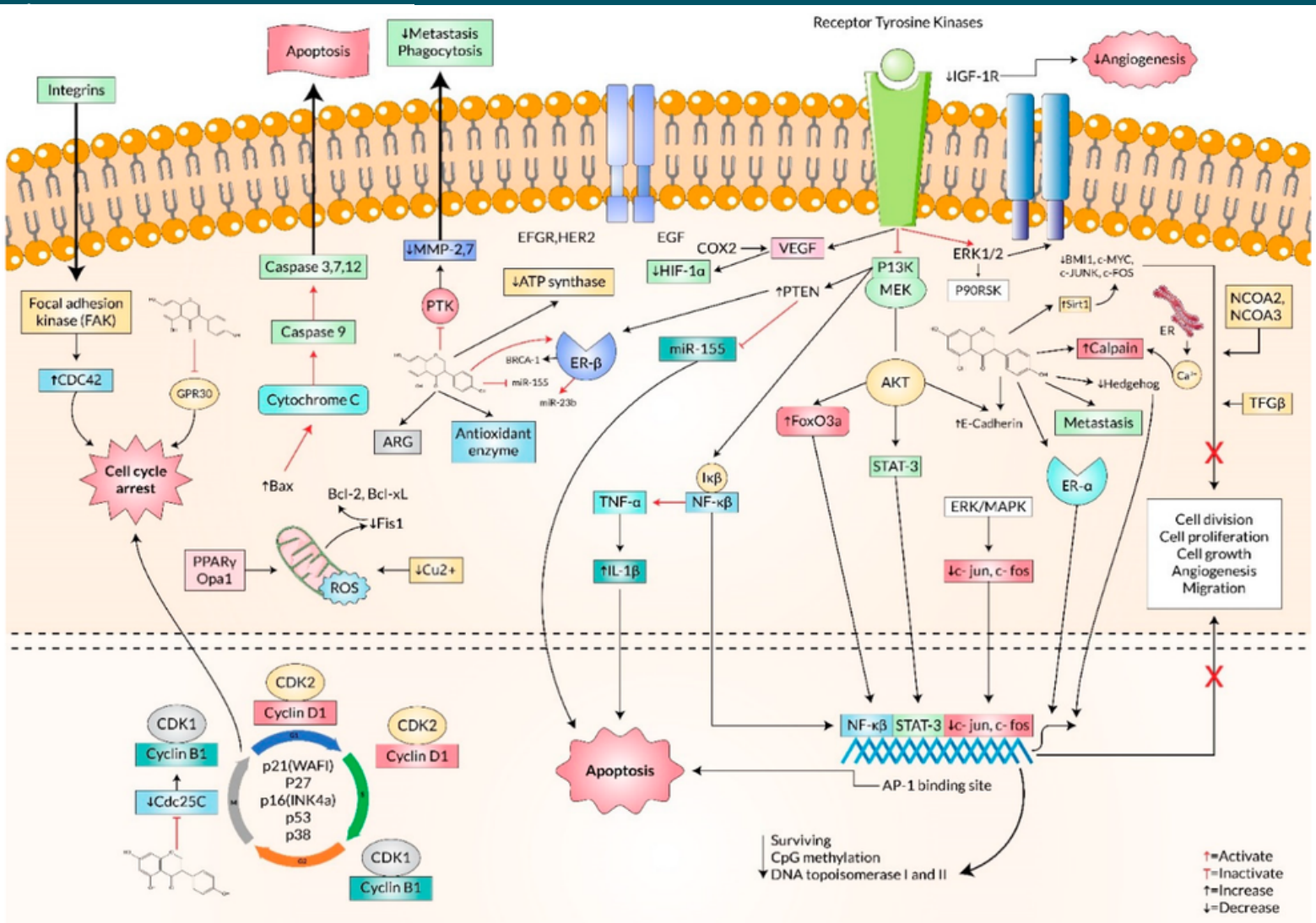


Figure B. Molecular targets of Genistein in breast cancer.

DOSE RECOMMENDED IN PUBLISHED CLINICAL TRAILS OF CANCER

560mg (8 mg/kg) genistein taken orally, is safe and can lead to plasma concentrations associated with anti-metastatic activity.

PUROBEST GENISTEIN RECOMMENDED DOSAGE

1-2 capsules of Purobest once a day or as directed by the healthcare practitioner.

Formulation Characteristics: Each purobest capsule contains 250mg of genistein. Quality of active ingredient is ensured via third party testing.

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