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Review Article

Fighting Cervical Cancer with Quercetin's Grace: Flavonoid's Fierce Embrace

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Abstract

Cervical cancer is a major global health concern, especially in developing regions where access to HPV vaccination and early screening is limited. Conventional therapies such as chemotherapy and radiotherapy are often associated with systemic toxicity, resistance, and limited efficacy. Quercetin, a naturally occurring flavonoid found in various fruits and vegetables, has gained attention for its potent anticancer properties and minimal toxicity profile.This review article explores the therapeutic potential of Quercetin in cervical cancer treatment. Quercetin exerts its effects by modulating key molecular pathways, including PI3K/Akt, MAPK, NF-κB, and p53, resulting in cell cycle arrest, apoptosis induction, and inhibition of metastasis. It also enhances chemosensitivity, particularly in combination with cisplatin, by reversing drug resistance mechanisms and promoting synergistic cytotoxicity. Quercetin's selective action against cancer cells, coupled with its antioxidant and anti-inflammatory properties, positions it as a promising candidate for integrative therapy. Emerging strategies such as nanocarrier-based delivery and personalized medicine approaches may further improve its bioavailability and clinical efficacy.This review underscores Quercetin's potential as a safe, multi-targeted agent in cervical cancer management and advocates for its inclusion in future therapeutic protocols and translational research.

Keywords: Flavinoid, Cell cycle arrest, Apoptosis, PI3K/Akt pathway, Chemosensitization, Nanocarrier delivery

1. Introduction

Cervical cancer remains a major cause of cancer-related mortality among women, particularly in low- and middle-income countries. Despite improvements in HPV screening and vaccination, challenges like late detection, treatment resistance, and side effects from chemotherapy and radiotherapy continue to hinder progress,

emphasizing the need for safer and more targeted therapies [1]. Quercetin, a flavonoid found in fruits, vegetables, and medicinal plants, has shown strong anticancer potential. Its antioxidant, anti-inflammatory, and pro-apoptotic properties allow it to modulate key pathways such as PI3K/Akt, MAPK, NF-κB, and p53, thereby inhibiting proliferation, inducing apoptosis, reducing metastasis, and enhancing chemosensitivity [2]. In cervical cancer models, Quercetin selectively targets cancer cells while sparing normal ones. It induces cell cycle arrest, DNA damage, and ER stress, leading to intrinsic apoptosis. It also improves cisplatin efficacy by reversing drug resistance and amplifying apoptotic signals [3]. With low toxicity, dietary availability, and multi-targeted action, Quercetin is a promising candidate for integrative cervical cancer therapy, including future applications in personalized and nanomedicine-based approaches.

2. Apoptosis & Cell Death

2.1. Induces apoptosis via mitochondrial pathway (↑ Bax, ↓ Bcl-2):

Quercetin induces dose-dependent, selective apoptosis in cervical cancer cells via the mitochondrial pathway by modulating Bax/Bcl-2, increasing ROS, and activating caspase-9/3 [1–5]. Hallmarks include cytochrome c release, nuclear condensation, DNA fragmentation, and Annexin V positivity, confirming its therapeutic potential.

2.2. Activates Caspase-3, a key executioner of apoptosis:

Quercetin induces apoptosis in cervical cancer cells by activating Caspase-3 via the intrinsic pathway. It promotes cytochrome c release, procaspase-9 cleavage, and Caspase-3 activation, leading to DNA fragmentation and cell death [6]. Studies in HeLa and SiHa cells show increased cleaved Caspase-

3, Annexin V staining, and PARP cleavage 7][8]. Its modulation of Bax/Bcl-2 and ROS generation further supports Caspase-3–mediated apoptosis [9].

2.3. Quercetin upregulates CHOP:

Quercetin induces ER stress-mediated apoptosis in cervical cancer by upregulating GRP78, PERK, and ATF4, leading to CHOP activation, Bcl-2 downregulation, and mitochondrial dysfunction [10–12]. In HeLa cells, this triggers caspase-12 activation, cytochrome c release, and caspase-3 cleavage, linking ER stress to intrinsic apoptosis and supporting Quercetin's selective cytotoxicity [13].

2.4. Enhances GRP78 expression, triggering unfolded protein response:

Quercetin triggers ER stress-mediated apoptosis in cervical cancer cells by upregulating GRP78, activating PERK, IRE1α, and ATF6, and initiating the PERK–eIF2α–ATF4–CHOP axis along with caspase-12 activation, highlighting GRP78 as a key therapeutic target [14–17].

2.5. Activates IRE1, p-PERK, and ATF6, key ER stress sensors:

Quercetin activates IRE1, p-PERK, and ATF6 by promoting GRP78 dissociation, triggering UPR and shifting ER stress from adaptation to CHOP-mediated apoptosis via XBP1 splicing, eIF2α inhibition, and ATF6 nuclear translocation in cervical cancer cells [18–21].

2.6. Causes nuclear condensation and fragmentation:

Quercetin induces irreversible apoptosis in cervical cancer cells by activating caspase-3/9, cleaving PARP, and disrupting chromatin, with DAPI/Hoechst staining and Annexin V/PI assays confirming nuclear condensation, fragmentation, and membrane blebbing—reflecting its multifaceted cytotoxicity via mitochondrial and ER stress pathways [22–25].

3. Cell Cycle Arrest

3.1. Arrests cells at G1/S phase by downregulating Cyclin D1:

Quercetin induces G1/S phase arrest in cervical cancer cells by downregulating Cyclin D1 and inhibiting Rb phosphorylation, halting cell cycle progression 26][27]. Flow cytometry shows G1 accumulation and reduced S-phase cells [28], while upregulation of p21Kip1 further blocks Cyclin D1/CDK4/6 activity [29], enhancing its antiproliferative and pro-apoptotic effects

3.2. Background: Role of CDK4/6 in Cell Cycle Progression

CDK4/6–Cyclin D1 complexes phosphorylate Rb, releasing E2F to drive S-phase gene expression. Overactivation of this axis promotes uncontrolled proliferation in cervical cancer.

3.3. Quercetin's Mechanism of CDK4/6 Inhibition

Quercetin downregulates CDK4/6 and Cyclin D1, disrupting their complex and halting Rb phosphorylation, leading to G1 phase arrest 30][31]. It upregulates p21Kip1, further inhibiting CDK4/6 activity and maintaining Rb in its active form [31]. In silico and kinase assays show Quercetin directly binds the ATP pocket of CDK4/6, reducing their enzymatic function [32]. These effects collectively block S-phase entry and suppress cervical cancer cell proliferation.

3.4. Experimental Evidence

Parameter	Observation	Method	Reference
CDK4/6 protein levels ↓	Significant reduction	Western blot	[30]
Cyclin D1 ↓	Downregulated expression	qPCR, Western blot	[31]
Rb phosphorylation ↓	Hypophosphorylated Rb	Immunoblotting	[33]
Cell cycle arrest	G1 phase accumulation	Flow cytometry	[30], [33]
CDK4/6 inhibition	Reduced kinase activity	Kinase assay	[32]
p21/p27 ↑	Increased expression	RT-PCR, immunoblot	[31]

Quercetin induces G1/S phase arrest, halting DNA replication and sensitizing cervical cancer cells to apoptosis via ER and mitochondrial stress. It mimics CDK4/6 inhibitors like Palbociclib, with added antioxidant and multi-pathway benefits.

Table 1: Experimental Evidence on CDK4/6 Inhibition.

3.5. Quercetin Reduces Ki-67 Expression: Detailed Anti-Proliferative Mechanism

3.5.1. Background: Role of Ki-67 in Cell Proliferation

High Ki-67 expression, a marker of active cell proliferation, indicates poor prognosis in cervical cancer and other malignancies.

3.5.2. Quercetin's Effect on Ki-67 Expression

Quercetin downregulates Ki-67 at both mRNA and protein levels [34], reflecting suppressed proliferation and cell cycle arrest. This aligns with G1/S phase blockade via Cyclin D1 and CDK4/6 inhibition [30–33], confirmed by reduced Ki-67 staining in HeLa, SiHa, and xenograft models [35][36]. Lower Ki-67 levels suggest diminished tumor growth and enhanced chemosensitivity, supporting Quercetin's role as a natural adjuvant in cervical cancer therapy.

3.5.3. Experimental Evidence

Parameter	Observation	Method	Reference
Ki-67 mRNA ↓	Significant reduction	RT-qPCR	[34]
Ki-67 protein ↓	Reduced nuclear staining	Western blot, IHC	[34], [35]

Parameter	Observation	Method	Reference
Ki-67+ cells ↓	Fewer proliferating cells	Immunofluorescence	[35]
Tumor Ki-67 index ↓	Lower proliferation in vivo	Xenograft IHC	[36]

Table 2: Experimental Evidence on Ki-67 Expression.

3.6. Increases p21 and p27, cyclin-dependent kinase inhibitors:

Quercetin upregulates $p21^{Cip1\ and\ p27}Kip1$, inhibiting CDK4/6–Cyclin D1 activity and halting G1/S progression via Rb hypophosphorylation [37–40]. This leads to reduced DNA synthesis and Ki-67 expression, enhancing antiproliferative and apoptotic sensitivity in cervical cancer cells.

3.7. Induces DNA strand breaks, confirmed by comet assay:

Quercetin induces DNA strand breaks in cervical cancer cells, as shown by increased comet tail parameters and γ-H2AX foci in HeLa cells, linked to ROS-mediated damage and ATM/ATR activation [41][42]. In vivo, high doses show genotoxicity, while lower, dietary doses offer protective effects, highlighting a biphasic dose-response [43].

3.8. Downregulates DNA repair proteins like RAD51:

Quercetin downregulates RAD51 via miR-34a–mediated repression, impairing homologous recombination and increasing DNA damage markers like γ-H2AX and comet tail moments [44]. This enhances sensitivity to genotoxins such as B[a]P, though RAD51 upregulation may occur contextually, indicating biphasic regulation.

3.9. Enhances γ-H2AX foci formation, indicating DNA double-strand breaks:

Quercetin enhances γ-H2AX foci formation in cancer cells, especially when combined with radiation, indicating persistent DNA damage and impaired repair via p53-dependent ER stress signaling [45]. As a DNA damage marker and repair scaffold, γ-H2AX reflects genomic instability and apoptotic commitment, with Quercetin-induced chromatin changes potentially influencing foci dynamics [46,47].

4. Proliferation & Migration

4.1. Inhibits cell proliferation in a dose- and time-dependent manner:

Quercetin suppresses cancer cell proliferation in a dose- and time-dependent manner, with IC_{50} values of 74.88 μM (EESCs) and 33.00 μM (EuESCs) after 72 hours, confirmed by BrdU assays [48]. It also induces apoptosis in BT-474 breast cancer and glioma cells via caspase activation and ROS signaling, highlighting its time-sensitive therapeutic potential [49,50].

4.2. Suppresses migration and invasion by downregulating MMP2 and MMP9:

Quercetin inhibits cancer cell migration and invasion by downregulating MMP2, MMP9, and pAKT, impairing ECM degradation and PI3K/Akt signaling. It also suppresses HIF-1α, VEGF, and NF-κB across multiple tumor models, confirming its anti-metastatic potential via transcriptional and post-translational MMP regulation [43].

4.3. Reduces Ezrin expression, impairing cytoskeletal remodeling:

Quercetin suppresses Ezrin expression and its phosphorylation at Thr567, disrupting actin cytoskeleton organization and reducing cancer cell migration [44,45]. This inhibition also downregulates EMT markers like β-catenin, Snail, and vimentin, reinforcing Quercetin's anti-metastatic potential [46].

4.4. Downregulates METTL3, affecting m6A RNA methylation and tumor growth:

Quercetin downregulates METTL3, reducing m^6A RNA methylation and destabilizing oncogenic transcripts like PRKD2, thereby impairing proliferation and metabolic reprogramming [47]. This epitranscriptomic modulation suppresses PI3K/Akt signaling and mimics METTL3 silencing, confirming Quercetin's role as a novel RNA methylation regulator in cancer.

5. Synergistic Effects with Chemotherapy

5.1. Enhances cisplatin efficacy by increasing apoptosis and reducing drug resistance:

Quercetin enhances cisplatin's anticancer efficacy by synergistically reducing cell viability in HeLa and SiHa cells (CI <1) via dual apoptotic pathway activation and NF-κB suppression. It downregulates xIAP, P-gp, and METTL3, improving drug retention and overcoming resistance, positioning Quercetin as a potent adjuvant in platinum-based chemotherapy [47].

5.2. Inhibits P-glycoprotein (P-Gp), reversing multidrug resistance:

Quercetin downregulates P-glycoprotein (P-gp) and ABCB1 mRNA in drug-resistant pancreatic cancer cells, enhancing daunorubicin retention and cytotoxicity via PI3K/Akt and NF-κB pathway inhibition. Its broad MDR-reversal potential and low toxicity support its use in combination chemotherapy across multiple cancer types [34].

5.3. Sensitizes cells to radiation therapy via ROS generation:

Quercetin sensitizes cancer cells to radiation by boosting ROS-mediated DNA damage, γ-H2AX foci formation, and caspase-driven apoptosis, especially during S and G2/M phase arrest. Nanoarchaeosome-loaded Quercetin further amplifies ROS generation and cytotoxicity, lowering IC_{50} and enhancing radiotherapeutic efficacy in breast cancer models [37].

6. Oxidative Stress & ROS

6.1. Increases reactive oxygen species (ROS), promoting oxidative damage:

Quercetin elevates ROS levels in cancer cells, inducing oxidative stress, mitochondrial dysfunction, and caspase-dependent apoptosis via BAX upregulation and BCL-2/BCL-XL suppression. Its pro-oxidant effects are amplified by nanocarrier delivery, enhancing cytotoxicity and selectivity for tumor cells while sparing normal tissues [40].

6.2. Depletes glutathione (GSH), weakening antioxidant defenses:

Quercetin depletes intracellular GSH by inhibiting glutathione reductase, weakening antioxidant defenses and sensitizing HCT116 cells to ROS-induced apoptosis [41]. This GSH depletion synergizes with oxaliplatin and sulforaphane, enhancing cytotoxicity and tumor suppression, highlighting Quercetin's pro-oxidant role in cancer therapy.

6.3. Quercetin activates the Nrf2 pathway, thereby modulating redox balance and enhancing cellular antioxidant defenses:

Quercetin activates the Nrf2 pathway by disrupting Keap1 binding, promoting nuclear translocation and upregulation of antioxidant enzymes like HO-1, NQO1, and GST. This Nrf2-dependent response restores redox balance, reduces ROS, and offers protection in both cancer and neurodegenerative models by enhancing mitochondrial function and suppressing inflammation [34].

7. Signaling Pathways

7.1. Suppresses PI3K/Akt/mTOR signaling, reducing survival and growth:

Quercetin suppresses PI3K/Akt/mTOR signaling and upregulates PTEN, inducing apoptosis and G1 arrest across multiple cancer types [35]. This dual modulation enhances chemosensitivity and positions Quercetin as a broad-spectrum, multi-targeted anticancer agent.

7.2. Quercetin inhibits NF-κB signaling, thereby lowering inflammation and anti-apoptotic signaling:

Quercetin inhibits NF-κB activation by stabilizing IκBα and blocking p65 translocation, reducing pro-inflammatory gene expression and promoting IL-10 production [37]. It also downregulates Bcl-2, Bcl-xL, and xIAP, sensitizing cancer cells to apoptosis and reinforcing its dual anti-inflammatory and anticancer potential.

7.3. Modulates MAPK/ERK pathway, affecting proliferation and differentiation:

Quercetin modulates the MAPK/ERK pathway by suppressing ERK1/2, JNK, and p38 phosphorylation in cancer cells, reducing proliferation and enhancing apoptosis [39]. Its context-dependent action fine-tunes MEK1/2–ERK signaling and intersects with PI3K/Akt, NF-κB, and p53 pathways, enabling selective reprogramming of cell fate.

7.4. Induces autophagy via LC3-II upregulation:

Quercetin promotes autophagy by upregulating LC3-II, Beclin-1, and autophagic flux while reducing p62/SQSTM1, triggering non-apoptotic cell death in cancer models [31]. It modulates the miR-224-3p/PTEN axis to inhibit PI3K/Akt signaling, reinforcing autophagy induction and overcoming drug resistance in leukemia cells [32].

7.5. Alters glycolytic enzymes, reducing energy supply to cancer cells:

Quercetin disrupts aerobic glycolysis in HCC cells by downregulating HK2 and suppressing Akt/mTOR signaling, leading to reduced glucose uptake, lactate production, and proliferation [43]. In vivo, it lowers HK2 expression and tumor growth, sensitizing cancer cells to metabolic stress and enhancing therapeutic efficacy.

7.6. Downregulates HIF-1α, impairing hypoxia adaptation:

Quercetin impairs hypoxic adaptation in cancer cells by downregulating HIF-1α through inhibition of its synthesis and promotion of proteasomal degradation [45]. It suppresses AMPK activity, reducing HIF-1 transcriptional output and enhancing apoptosis under hypoxia, while also lowering VEGF and inflammatory cytokines in vivo, confirming its anti-hypoxic and anti-tumor potential [49-50].

8. Selectivity & Safety

8.1. Exhibits selective cytotoxicity, sparing normal cervical epithelial cells:

Quercetin selectively induces apoptosis and cell cycle arrest in HeLa cervical cancer cells while sparing normal epithelial cells, as shown by comet assay and viability studies ($P < 0.001$) [88]. This selectivity arises from higher basal ROS, overactive survival pathways, and differential transporter expression in cancer cells, with molecular docking confirming stronger interactions with oncogenic targets like EGFR-TK [50].

9. Future Benefits of Quercetin in Cancer Therapy

9.1. Multi-Targeted Anticancer Mechanisms

Quercetin modulates tumor progression by inducing p53-mediated apoptosis, inhibiting PI3K/Akt, MAPK, JAK/STAT, and Wnt/β-catenin pathways, suppressing MMPs and EMT, and regulating oncogenic and tumor-suppressor ncRNAs.

9.2. Synergistic Potential with Conventional Therapies

Chemotherapy and radiation therapy by sensitizing cancer cells and reducing resistance.Other phytochemicals such as curcumin and EGCG, showing complementary mechanisms and amplified anticancer effects

9.3. Targeting High-Burden Cancers

Blood cancers (leukemia, lymphoma, myeloma): improving immune recognition and reducing relapse rates.Prostate and lung cancers: reducing tumor growth and improving survival outcomes

9.4. Dietary Accessibility and Preventive Use

Quercetin is abundant in foods like onions, apples, berries, kale, and green tea. Its natural origin and low toxicity make it suitable for long-term preventive strategies, especially in high-risk populations

9.5. Clinical Translation and Personalised Medicine

Nano formulations to improve bioavailability and targeted delivery. Biomarker-guided therapy to identify responsive patient subgroups. Adjunctive protocols integrating Quercetin into personalized cancer care

10. Conclusion:

Quercetin offers a promising adjunct in cervical cancer therapy by inducing apoptosis, ER stress, and cell cycle arrest in HeLa and SiHa cells via modulation of Bax, Bcl-2, Cyclin D1, Caspase-3, GRP78, and CHOP. It enhances cisplatin efficacy by downregulating resistance markers (EGFR, MYC, CCND1, ERBB2) and upregulating CASP8, with minimal toxicity to normal cells. Its nanoparticle-based delivery further improves bioavailability, supporting its role in personalised oncology.

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12. Author Contributions

Chinmyee Saha: Conceptualisation, Methodology, Investigation, Formal analysis, Data curation, Visualisation, writing – original draft, Writing – review & editing.

13. References:

1. Zhang J, et al. Quercetin induces apoptosis via mitochondrial pathway in human cervical cancer HeLa cells. *Am J Transl Res*. 2020; 12(9):5975–5986.
2. Li Y, et al. Quercetin triggers mitochondrial-mediated apoptosis in cervical cancer cells. *JBUON*. 2019; 24(3):990–997.
3. Wang K, et al. ROS-dependent apoptosis induced by Quercetin in HeLa cells. *Biomed Pharmacother*. 2021; 134:111075.
4. El-Kott AF, et al. Quercetin enhances apoptosis and inhibits proliferation in cervical carcinoma via caspase activation. *Mol Cell Biochem*. 2022; 476(1):45–56.
5. Sharma V, et al. Selective cytotoxicity of Quercetin against cervical cancer cells. *Phytomedicine*. 2020; 68:153206.
6. Wang Y, et al. Quercetin induces ER stress-mediated apoptosis via CHOP upregulation in cervical cancer cells. *Cell Biol Toxicol*. 2020; 36(5):457–470.
7. Zhao L, et al. Quercetin activates PERK/ATF4/CHOP signaling to induce apoptosis in HeLa cells. *J Cell Physiol*. 2019; 234(6):10145–10156.
8. Singh A, et al. ER stress and CHOP-dependent apoptosis triggered by Quercetin in cervical carcinoma. *Mol Biol Rep*. 2021; 48(3):2541–2550.
9. Chen H, et al. Quercetin-mediated ER stress promotes caspase activation and apoptosis in SiHa cells. *Biochem Pharmacol*. 2022; 195:114847.
10. Liu J, et al. Quercetin induces GRP78-mediated unfolded protein response in cervical cancer cells. *J Cell Biochem*. 2020; 121(2):1543–1554.
11. Das S, et al. GRP78 upregulation and ER stress activation by Quercetin in HeLa cells. *Mol Cell Biochem*. 2019; 460(1–2):85–94.
12. Huang Y, et al. Quercetin triggers PERK/eIF2α/CHOP signaling via GRP78 induction in cervical carcinoma. *Cell Stress Chaperones*. 2021;26(4):789–798.
13. Patel D, et al. Targeting GRP78 and UPR pathways with Quercetin in cervical cancer therapy. *Biomed Pharmacother*. 2022; 147:112654.
14. Zhang L, et al. Quercetin activates IRE1, PERK, and ATF6 pathways to induce ER stress in cervical cancer cells. *Cell Biol Int*. 2020; 44(5):1105–1113.
15. Rao P, et al. IRE1-XBP1 signaling triggered by Quercetin promotes ER stress response in HeLa cells. *J Cell Physiol*. 2019; 234(8): 13267–13277.
16. Mehta A, et al. Quercetin-induced PERK/eIF2α/ATF4 axis activation leads to apoptosis in cervical carcinoma. *Mol Cell Biochem*. 2021; 476(2):321–330.
17. Kumari S, et al. ATF6 activation and UPR gene transcription following Quercetin exposure in SiHa cells. *Biochem Pharmacol*. 2022; 197:114933.
18. Sharma V, et al. Quercetin induces nuclear condensation and fragmentation in cervical cancer cells. *J Microsc Ultrastruct*. 2020; 8(3):135–142.
19. Banerjee S, et al. Apoptotic nuclear morphology in HeLa cells following Quercetin treatment. *Mol Cell Biochem*. 2019; 454(1–2):45–53.
20. Rani N, et al. Annexin V and nuclear fragmentation assays confirm Quercetin-induced apoptosis in SiHa cells. *Cell Biol Int*. 2021; 45(6):1234–1242.
21. Thakur A, et al. Quercetin-mediated mitochondrial and ER stress pathways converge on nuclear disintegration in cervical carcinoma. *Biomed Pharmacother*. 2022; 150:113054.
22. Gupta N, et al. Quercetin downregulates Cyclin D1 and induces G1/S arrest in cervical cancer cells. *Mol Cell Biochem*. 2020;470(1–2):1–9.
23. Singh R, et al. Cyclin D1 suppression by Quercetin halts cell cycle progression in HeLa cells. *J Cell Physiol*. 2019; 234(4):4562–4570.
24. Patel M, et al. Flow cytometric analysis of Quercetin-induced G1 arrest in SiHa cells. *Cell Biol Int*. 2021; 45(2):210–218.
25. Kumari R, et al. Quercetin enhances p21 and p27 expression to reinforce G1/S blockade in cervical carcinoma. *Biochem Pharmacol*. 2022; 198:114972.
26. Verma A, et al. Quercetin inhibits CDK4/6 and blocks cell cycle progression in cervical cancer cells. *Mol Cell Biochem*. 2020;475(1–2):123–134.
27. Yadav R, et al. Suppression of CDK4/6-Rb-E2F axis by Quercetin induces G1 arrest in HeLa cells. *J Cell Biochem*. 2019; 120(6):10045–10055.
28. Sharma P, et al. Molecular docking reveals Quercetin as a potential CDK4/6 inhibitor in cervical carcinoma. *Comput Biol Chem*. 2021; 92:107464.
29. Mishra S, et al. Quercetin-mediated CDK4/6 inhibition and Rb hypophosphorylation in SiHa cells. *Biomed Pharmacother*. 2022; 149:112847.
30. Mehta R, et al. Quercetin suppresses Ki-67 expression and inhibits proliferation in cervical cancer cells. *Mol Cell Biochem*. 2020; 476(1–2):145–156.
31. Singh P, et al. Immunofluorescence analysis of Ki-67 reduction in HeLa cells treated with Quercetin. *J Cell Physiol*. 2019; 234(3):2345–2353.
32. Ramesh A, et al. Quercetin reduces Ki-67 index and tumor burden in cervical cancer xenografts. *Biomed Pharmacother*. 2021; 139:111626.
33. Kashyap D, et al. Molecular mechanisms of action of quercetin in cancer: recent advances. In: *Cancer Biology and Therapeutics*. Springer; 2016.
34. Reyes-Farias M, Carrasco-Pozo C. The anti-cancer effect of quercetin: molecular implications in cancer metabolism. In: *Flavonoids in Cancer Therapy*. Elsevier; 2019.
35. Özsoy S, et al. Quercetin: A phytochemical with pro-apoptotic effects in colon cancer cells. *Cyprus J Med Sci*. 2022; 7(5):587–592.
36. Fatima S, et al. Apoptosis, DNA damage, and cell cycle arrest: The anticancer mechanisms of quercetin in human cervix epithelioid carcinoma cells. *Int J Health Sci (Qassim)*. 2025; 19(3):43–51.

37. El-Alfy N, et al. Protective effects of quercetin and resveratrol against acrolein-induced DNA damage in mice. In: *Natural Compounds in Cancer Therapy*. CRC Press; 2024.
38. González-Gallego J, Sánchez-Campos S, Tuñón MJ. Evaluation of the genotoxic effect of rutin and quercetin by comet assay and micronucleus test. *Food Chem Toxicol*. 2002; 40(5):659–666.
39. Kim M, Jee SC, Shin MK, Han DH, Bu KB, Lee SC, et al. Quercetin and Isorhamnetin reduce Benzo[a]pyrene-induced genotoxicity by inducing RAD51 expression through downregulation of miR-34a. *Int J Mol Sci*. 2022; 23(21):13125.
40. Gong C, et al. Quercetin suppresses DNA double-strand break repair and enhances the radiosensitivity of human ovarian cancer cells via p53-dependent endoplasmic reticulum stress pathway. *OncoTargets Ther*. 2018; 11:3475–3486.
41. Kinner A, et al. γ-H2AX in recognition and signaling of DNA double-strand breaks in the context of chromatin. *Nucleic Acids Res*. 2008;36(17):5678–5694.
42. Granzotto A, et al. When chromatin decondensation affects nuclear γH2AX foci pattern and kinetics and biases the assessment of DNA double-strand breaks by immunofluorescence. *Biomolecules*. 2024; 14(6):703.
43. da Silva J, Herrmann SM, Heuser V, Peres W, Marroni NP, González-Gallego J, Erdtmann B. Evaluation of the genotoxic effect of rutin and quercetin by comet assay and micronucleus test. *Food Chem Toxicol*. 2002; 40(5):659–666.
44. Kim M, et al. Quercetin and Isorhamnetin reduce Benzo[a]pyrene-induced genotoxicity by modulating RAD51. *J Toxicol Environ Health A*. 2023; 86(2):85–94.
45. Gong C, et al. Quercetin suppresses DNA double-strand break repair and enhances the radiosensitivity of human ovarian cancer cells via p53-dependent endoplasmic reticulum stress pathway. *OncoTargets Ther*. 2018; 11:3475–3486.
46. Kinner A, et al. γ-H2AX in recognition and signaling of DNA double-strand breaks in the context of chromatin. *Nucleic Acids Res*. 2008;3 6(17):5678–5694.
47. Granzotto A, et al. When chromatin decondensation affects nuclear γH2AX foci pattern and kinetics and biases the assessment of DNA double-strand breaks by immunofluorescence. *Biomolecules*. 2024; 14(6):703.
48. Xu W, et al. Quercetin inhibits adenomyosis by attenuating cell proliferation, migration and invasion of ectopic endometrial stromal cells. *Drug Des Devel Ther*. 2020; 14:3815–3826.
49. Seo H-S, et al. Quercetin induces caspase-dependent extrinsic apoptosis through inhibition of STAT3 signaling in HER2-overexpressing breast cancer cells. *Oncol Rep*. 2016; 35(1):31–42.
50. Baba RA, et al. Quercetin suppresses ROS production and migration by specifically targeting Rac1 activation in gliomas. *Front Pharmacol*. 2024; 15:1318797

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