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Epigallocatechin-3-Gallate Triggers Mitochondrial-Mediated Apoptosis and Suppresses EGFR Signaling in Cervical Cancer Cells

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Abstract

Background: Cervical cancer is associated with a relatively high mortality rate in women. Conventional therapies often cause significant adverse effects, highlighting the need for novel treatments with improved safety and efficacy.

Objectives: Considering that epigallocatechin-3-gallate (EGCG) has anticancer effects in various malignancies, this study evaluated the impacts of EGCG on cervical cancer cells, with emphasis on identifying the mechanism of action.

Methods: After culture, HeLa and CaSki cells were exposed to a range of EGCG concentrations. The MTT assay was used to assess cell viability, and flow cytometry was used for apoptosis. Finally, using designed primers, expression levels of *bax*, *CASP3*, *p53*, *bcl-2*, *CASP9*, and *EGFR* were quantified by qRT-PCR.

Results: The EGCG decreased cell viability in both cervical cancer cell lines and increased apoptosis. Notably, at 40 and 80 µg/mL, EGCG upregulated pro-apoptotic genes (*bax*, *p53*, *CASP3*, *CASP9*) and downregulated anti-apoptotic *bcl-2* and *EGFR* expression.

Conclusions: Our findings indicate that EGCG exerts anticancer activity against cervical cancer cell lines, at least in part, by activating the intrinsic mitochondrial apoptosis pathway as well as inhibiting proliferative signaling. Further mechanistic research is needed to determine the full spectrum of EGCG's actions in cervical cancer.

Keywords: Cervical Cancer, HeLa Cell, CaSki Cell, Apoptosis

1. Background

Cervical cancer is one of the most common malignancies in women, and its occurrence is expected to rise in the coming years (1). Human papillomavirus (HPV) infection, immunosuppression, smoking, and prolonged use of combined contraceptives are among the risk factors for cervical cancer, with HPV infection representing the greatest risk factor (2).

Treatment approaches vary according to cancer stage, tumor size, metastasis, and histology, as well as patient-related factors such as age and pregnancy status (3). Surgery — including cone biopsy, radical hysterectomy, and radical or pelvic lymphadenectomy — represents a primary treatment modality (4). However, surgical management can be associated with complications such as infection, bladder or rectal injury, and premature menopause (5). Additionally, other modalities such as radiotherapy, chemotherapy, and immunotherapy are employed in the management of cervical cancer; these treatments can have significant side effects that adversely affect quality of life (6). Therefore, the ongoing development of novel therapeutic strategies is of great importance

In the last two decades, research has increasingly explored the effects of natural products on a wide range

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of cancers, with several compounds showing potential anticancer activity (7). Epigallocatechin-3-gallate (EGCG) has shown anti-proliferative effects across multiple cancer types (8, 9). The EGCG is extracted from green tea extract (10) and has a broad spectrum of pharmacological characteristics, including antioxidant, anti-obesity, anti-inflammatory, and anticancer effects (11). The EGCG can modulate cancer-relevant signaling pathways, including EGFR-JAK/STAT, PI3K/AKT/mTOR, and MAPK/ERK pathways (12). In cervical cancer, EGCG has been reported to inhibit metastasis by affecting reactive oxygen species (ROS) dynamics (13), and in lung cancer, it has been shown to reduce invasion and metastasis via inhibition of EGFR signaling (14). Additionally, EGCG demonstrates anticancer impact on colorectal cancer by targeting cellular metabolism (15).

2. Objectives

This study aims to investigate the anticancer effects of EGCG in a cervical cancer cell model, with an emphasis on identifying the mechanisms of action of this natural product.

3. Methods

3.1. Cell Line Preparation and Culture

HeLa (ATCC No. CCL-2) and CaSki (ATCC No. CRL-1550TM) cell lines were obtained from the Pasteur Institute of Iran and cultured in RPMI1640 medium supplemented with 10% FBS and penicillin and streptomycin antibiotics. T25 flasks containing cells were incubated at 37°C and 5% CO_2.

3.2. Cell Viability

The EGCG was purchased from Merck (CAS# 989-51-5, Germany) (dissolved in 0.1% DMSO v/v). Cells (10^5 per well) were cultured in 96-well plates and exposed to 5 to 80 µg/mL EGCG and incubated for 72 hours at 37°C. Then, 5 mg/mL MTT solution (Sigma) was added to the cells and incubated again for 4 hours under the above conditions, and finally, after adding 50 µL DMSO, OD was read at 570 nm.

3.3. Cell Apoptosis

The apoptosis rate of cells was measured using a flow cytometry device and the FITC Annexin V commercial kit (BD Biosciences) according to the manufacturer's instructions. The gating strategy included the sum of early apoptotic cells (positive for Annexin V and negative for PI) and late apoptotic cells (positive for both Annexin V and PI).

3.4. Gene Expression

RNAs from HeLa and CaSki cancer cells were purified using the QIAwave RNA Mini Kit (CAT# 74534, QiaGene, Germany), and after confirming its suitable quantity and quality, the cDNA was synthesized via the cDNA Synthesis Kit (ThermoFisher, USA). Primer sequences for *bcl-2*, *CASP3*, *bax*, *CASP9*, *p53*, and *EGFR* genes were designed in Primer3 software and validated by blasting on the NCBI website. Primer sequences are given in Table 1.

Table 1. The Primer Sequences Used in this Study to Measure the Expression Levels of *casp3*, *cap9*, *p53*, *bax*, *bcl-2*, and *EGFR* Genes

Genes	Sequence [5'-3']
bax	
F	GTGGATGACTGAGTACCTGAAC
R	GCCAGGAGAAATCAAACAGAGG
CASP3	
F	TGGAAAATCCCAGAAAGATCTG
R	AGGGCAAATTCCAGTTTCCT
CASP9	
F	GTTTGAGGACCTTCGACCAGCT
R	CAACGTACCAGGAGCCACTCTT
bcl-2	
F	GAGCAGATCATGAAGACAGGG
R	ATGCGCTTGAGACACTCG
P53	
F	CCTCAGCATCTTATCCGAGTGG
R	TGGATGGTGGTACAGTCAGAGC
EGFR	
F	AACACCCTGGTCTGGAAGTACG
R	TCGTTGGACAGCCTTCAAGACC
GAPDH	
F	TTGGCTACAGCAACAGGGTG
R	GGGGAGATTCAGTGTGGTGG

The qRT-PCR reaction mixture consisted of 0.5 µL each of reverse and forward primers, 10 µL Master Mix, 2 µL cDNA, and 7 µL deionized water (final volume: 20 µL). In addition, the instrument program included three cycles, the first of which was 95°C for 15 min for denaturation, and the second consisted of 40 cycles of 95°C for 15 s and 60°C for 60 s, and a final cycle of 72°C for 10 min. The gene expression data were analyzed using the $2^{-\Delta\Delta CT}$ method and normalized by the expression of the control gene (GAPDH).

3.5. Statistical Analysis

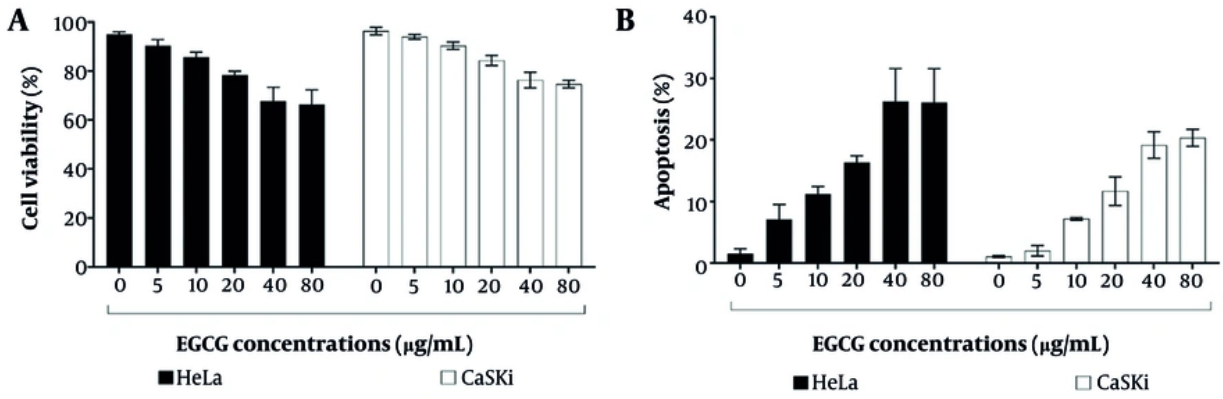

Figure 1. The viability of HeLa and CaSki cell lines (A) and the apoptosis rate (B) after treatment with 0, 5, 10, 20, 40, and 80 µg/mL epigallocatechin-3-gallate (EGCG). Cells were treated with EGCG for 72 hours, and cell viability and apoptosis were measured by MTT assay and flow cytometry, respectively (n = 3).

The Shapiro-Wilk test was used for checking the normal distribution of the data. Variables with a normal distribution were analyzed using two-way analysis of variance (ANOVA), and nonparametric tests were used to analyze non-normal variables, followed by pairwise comparisons using Tukey's test by considering $P < 0.05$ as the significance level. Data were analyzed in GraphPad Prism V.8 software.

4. Results

4.1. Cell Viability and Apoptosis Rate

The EGCG significantly reduced cancer cell viability at concentrations of 10 µg/mL (HeLa-MD: 9.33%, 95% CI: 1.85 to 16.8%, P = 0.008), 20 µg/mL (HeLa-MD: 16.67%, 95% CI: 9.19 to 24.15%, P < 0.001; CaSki-MD: 12%, 95% CI: 4.52 to 19.48%, P < 0.001), 40 µg/mL (HeLa-MD: 27.33%, 95% CI: 19.85 to 34.81%, P < 0.001; CaSki-MD: 20.0%, 95% CI: 12.52 to 27.48%, P < 0.001), and 80 µg/mL (HeLa-MD: 28.67%, 95% CI: 21.9 to 36.15%, P < 0.001; CaSki-MD: 21.67%, 95% CI: 14.19 to 29.15%, P < 0.001) relative to untreated control cells (Figures 1 and 2). The greatest reductions in viability were observed with 80 and 40 µg/mL EGCG; however, there was no statistically significant difference in viability between the 40 µg/mL and 80 µg/mL EGCG treatments for either cancer line (HeLa-MD: 1.33%, 95% CI: -6.15 to 8.81, P = 0.932; CaSki-MD: 1.67%, 95% CI: -5.81 to 9.15, P = 0.981).

Additionally, EGCG exposure significantly increased the apoptosis rate in cells. A significant rise in apoptosis was observed in HeLa cells at 10 µg/mL (P = 0.001) and at 20, 40, and 80 µg/mL (P < 0.0001). In CaSki cells, the increase in apoptosis at 10 µg/mL EGCG was not statistically significant (P = 0.075). Notably, there was no significant difference in the percentage of apoptosis between the two cervical cancer cell lines when exposed to 80 or 40 µg/mL EGCG (Figures 1 and 2).

4.2. Gene Expressions

4.2.1. bax and bcl-2

Both HeLa and CaSki cervical cancer cell lines showed overexpression of *bax* in response to EGCG, whereas *bcl-2* was downregulated. In HeLa cells, EGCG at concentrations of 10 µg/mL (MD: -0.206, 95% CI: -0.399 to -0.014, P = 0.030), 20 µg/mL (MD: -0.706, 95% CI: -0.899 to -0.513, P < 0.001), 40 µg/mL (MD: -0.904, 95% CI: -1.097 to -0.711, P < 0.001), and 80 µg/mL (MD: -0.893, 95% CI: -1.097 to -0.711, P < 0.001) significantly upregulated *bax* compared with untreated cells. Similarly, CaSki cells showed significant bax overexpression in response to 10 (P = 0.047), 20, 40, and 80 µg/mL (P < 0.001) EGCG. Notably, the highest *bax* expression was observed at 40 and 80 µg/mL EGCG in both cervical cancer cell lines (Figure 3A).

Conversely, treatment with EGCG was associated with downregulation of *bcl-2*. In HeLa cells, exposure to 20 µg/mL (MD: 0.334, 95% CI: 0.150 to 0.517, P < 0.001), 40 µg/mL (MD: 0.533, 95% CI: 0.349 to 0.716, P < 0.001), and 80 µg/mL (MD: 0.529, 95% CI: -0.158 to 0.208, P < 0.001) EGCG resulted in significantly reduced *bcl-2* expression compared with untreated cells (Figure 3B). Similarly, CaSki cells exhibited decreased *bcl-2* expression in response to EGCG at 20 µg/mL (MD: 0.365, 95% CI: 0.182 to

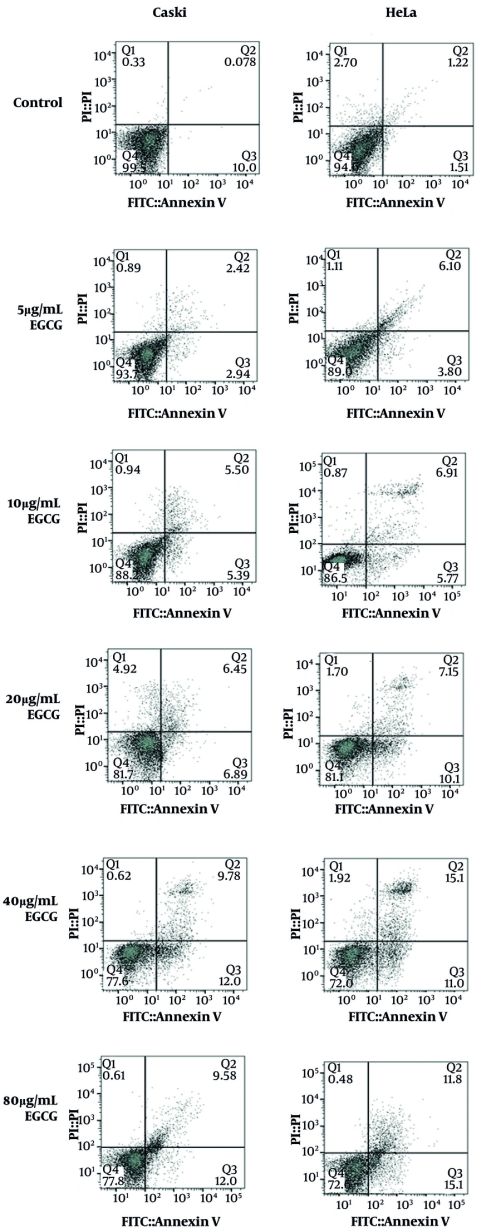

Figure 2. Histograms obtained from flow cytometry to measure the rates of apoptosis in the cervical cancer cells

0.549, P < 0.001), 40 µg/mL (MD: 0.467, 95% CI: 0.284 to 0.651, P < 0.001), and 80 µg/mL (MD: 0.502, 95% CI: 0.319 to 0.682, P < 0.001).

4.2.2. CASP3 and CASP9

Caspase-3 (*CASP3*) gene expression in HeLa cells was significantly upregulated by 40 µg/mL EGCG [mean difference (MD): -0.342, 95% CI: -0.583 to -0.100, P = 0.0025] and 80 µg/mL (MD: -0.346, 95% CI: -0.588 to -0.110, P = 0.0022). By contrast, EGCG at 5 µg/mL (P = 0.973), 10 µg/mL (P = 0.560), and 20 µg/mL (P = 0.165) had

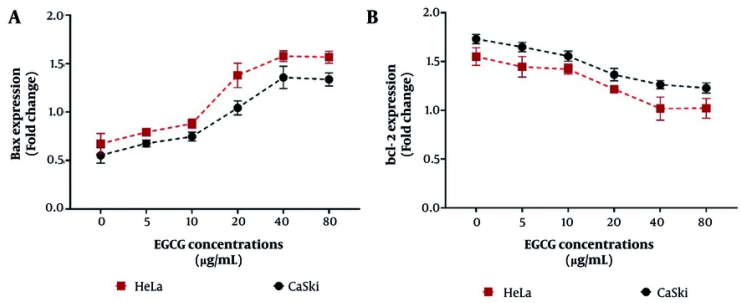

Figure 3. The expression of *bax* (A) and *bcl-2* (B) genes in HeLa and CaSki cell lines after treatment with 0, 5, 10, 20, 40, and 80 µg/mL epigallocatechin-3-gallate (EGCG). Cells were treated with EGCG for 72 hours, and gene expression was measured by qRT-PCR (n = 3).

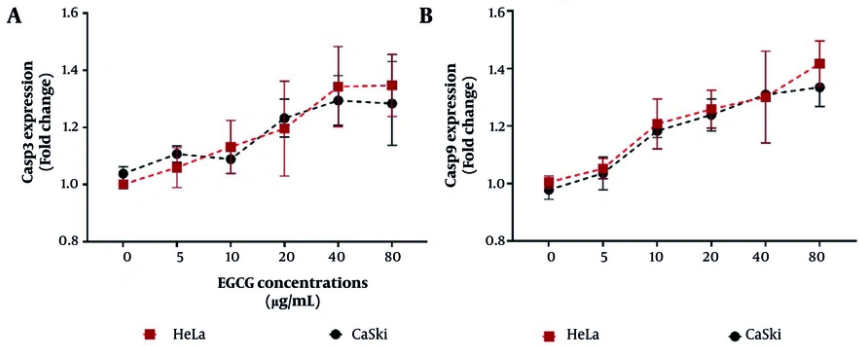

Figure 4. The expression of *CASP3* (A) and *CASP9* (B) genes in HeLa and CaSki cell lines after treatment with 0, 5, 10, 20, 40, and 80 µg/mL epigallocatechin-3-gallate (EGCG). Cells were treated with EGCG for 72 hours, and gene expression was measured by qRT-PCR (n = 3).

no significant effect on *CASP3* expression in HeLa cells. In CaSki cells, *CASP3* expression was significantly upregulated only at 40 µg/mL (MD: -0.256, 95% CI: -0.498 to -0.014, P = 0.033) and 80 µg/mL (MD: -0.245, 95% CI: -0.487 to -0.003, P = 0.044) compared with untreated cells (Figure 4A).

CASP9 was significantly overexpressed in both HeLa and CaSki cells when exposed to: 10 µg/mL (HeLa: P = 0.017; CaSki: P = 0.015), 20 µg/mL (HeLa: P = 0.002; CaSki: P = 0.001), 40 µg/mL (HeLa: P < 0.001; CaSki: P < 0.0001), and 80 µg/mL (HeLa: P < 0.0001; CaSki: P < 0.0001) EGCG, relative to untreated cells (Figure 4B).

4.2.3. p53 and EGFR

Both HeLa and CaSki cells upregulated *p53* expression in response to exposure to EGCG at 10–80 µg/mL, with the highest *p53* expression observed in cancer cells exposed to 40 and 80 µg/mL EGCG (Figure 5A). In contrast, these cervical cancer cell lines downregulated *EGFR* expression in response to EGCG at 20 µg/mL (HeLa: P = 0.007; CaSki: P = 0.003), 40 µg/mL (P < 0.001), and 80 µg/mL (P < 0.0001). The lowest *EGFR* expression was quantified in the cells treated with 40 µg/mL (HeLa: MD = 0.454; CaSki: MD = 0.340) and 80 µg/mL EGCG (HeLa: MD = 0.441; CaSki: MD = 0.363) (Figure 5B).

5. Discussion

Cervical cancer, as a common malignancy, is associated with substantial mortality and morbidity (16). Key therapeutic modalities include surgery, radiotherapy, chemotherapy, and immunotherapy; each is linked to notable adverse effects (17), which necessitates the development of new therapeutic approaches. In this research, we evaluated the impacts

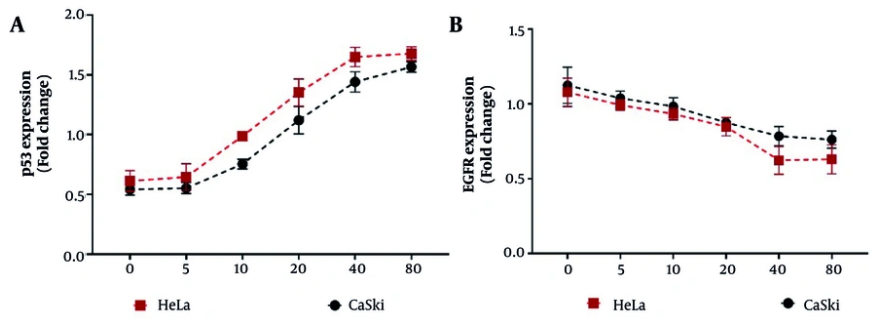

Figure 5. The expression of *p53* (A) and *EGFR* (B) genes in HeLa and CaSki cell lines after treatment with 0, 5, 10, 20, 40, and 80 µg/mL epigallocatechin-3-gallate (EGCG). Cells were treated with EGCG for 72 hours, and gene expression was measured by qRT-PCR (n = 3).

of varying concentrations of EGCG on two cervical cancer cell lines, HeLa and CaSki. Our findings show that EGCG exerts cytotoxic effects, particularly at higher concentrations (40 and 80 µg/mL), against cancer cells, and cancer cell death was accompanied by apoptosis. Gene expression analysis revealed that EGCG upregulated *bax*, *CASP3*, *CASP9*, and *TP53* (*p53*) transcripts, while downregulating *bcl-2* and *EGFR* transcripts in cancer cells. Collectively, these results suggest that the cytotoxic effects of EGCG are mediated, at least in part, by activation of the mitochondrial (intrinsic) apoptotic pathway and by inhibition of proliferative signaling via the EGFR pathway.

The EGCG is one of the most important catechin compounds in several plants, particularly green tea, and has shown a broad spectrum of biological effects, including antioxidant, anti-obesity, anti-inflammatory, anti-diabetic, and anticancer effects (18). The anticancer activities of this natural product are exerted through modulation of multiple signaling pathways (12). In this study, we observed that EGCG exerted anticancer effects against both HeLa and CaSki cervical cancer cell lines, accompanied by the induction of apoptosis. Our findings align with numerous studies reporting anticancer effects of EGCG across a variety of malignancies (19-21). Notably, in this study, 40 µg/mL EGCG had strong cytotoxic effects against both ovarian cancer cell lines. This contrasts with Zhang et al., who reported that 80 µg/mL EGCG induced maximal cell death in hepatocellular carcinoma HCCLM6 cells, suggesting cell-type–specific sensitivity to EGCG (22). Differences in cell type may account for this discrepancy, indicating that HeLa and CaSki cells may be more sensitive to EGCG. Another study reported that 40 µg/mL EGCG significantly inhibited proliferation of Hep3B cells (23), consistent with our observation that this concentration can induce substantial cytotoxic effects.

This study showed that EGCG overexpressed *bax*, *CASP3*, *CASP9*, and *p53* genes, while downregulating *bcl-2* and *EGFR* in cancer cells. These findings indicated that EGCG promotes a shift toward pro-apoptotic signaling in cancer cells, as evidenced by the upregulation of *bax*, *CASP3*, *CASP9*, and *p53* transcripts alongside the downregulation of anti-apoptotic *bcl-2* and the growth/survival receptor *EGFR*. Increased *bax* can disrupt mitochondrial membrane integrity, facilitating cytochrome c release and activation of the caspase cascade, highlighted by elevated *CASP9* and *CASP3* transcriptional signals (24). The concurrent rise in *p53* suggests a p53-mediated transcriptional response to cellular stress, reinforcing apoptotic pathways and potentially enhancing DNA damage surveillance (25, 26). Suppression of *bcl-2* removes a critical brake on mitochondrial outer membrane permeabilization, synergizing with Bax to promote apoptosis (27). Reduced EGFR transcripts may diminish proliferative and survival signaling, further tipping the balance toward cell death rather than growth (28, 29). Collectively, these gene expression changes support a mechanistic model where EGCG activates intrinsic apoptosis and suppresses pro-survival cues, offering a molecular rationale for its anticancer effects in this context.

It seems that EGCG elicits a dose-dependent alteration of key regulatory pathways in cervical cancer cells, upregulating the tumor suppressor p53 while concurrently suppressing the receptor tyrosine kinase EGFR. The concordant changes in p53 and EGFR expression may reflect a coordinated cellular response to EGCG that contributes to reduced proliferation and

increased apoptotic signaling in these cell lines. However, this study was conducted *in vitro*, which is one of the limitations of this study, and generalization of the findings of this research to clinical conditions should be done with caution. Therefore, further mechanistic studies are warranted to dissect the upstream regulators mediating EGCG's effects on p53 and EGFR expression. Finally, functional validation (protein levels) would strengthen the link between transcript changes and cell fate.

5.1. Conclusions

Our data indicate that EGCG exerts dose-dependent cytotoxic effects on cancer cells, with the most pronounced cell death observed at higher concentrations (40 and 80 µg/mL), predominantly via apoptosis. The observed transcriptional profile supports activation of the intrinsic (mitochondrial) apoptotic pathway, evidenced by upregulation of pro-apoptotic *bax*, caspases (*CASP3* and *CASP9*), and *p53*, together with downregulation of anti-apoptotic *bcl-2*. Concurrent suppression of EGFR suggests reduced pro-survival signaling, which may further sensitize cells to apoptotic death. Collectively, these results propose a mechanistic model in which EGCG initiates mitochondrial-dependent apoptosis and attenuates growth/survival pathways in cancer cells. Future studies validating these findings at the protein level and assessing functional apoptosis will strengthen the translational potential of EGCG as an anticancer agent.

Footnotes

AI Use Disclosure: The authors declare that no generative AI tools were used in the creation of this article.

Authors' Contribution: Study concept and design: M. Z. M. and K. A.; Analysis and interpretation of data: S. Z. M. and Z. G.; Drafting of the manuscript: Z. G.; Critical revision of the manuscript for important intellectual content: M. Z. M., H. G., K. A., and S. Z. M.; Statistical analysis: H. G.

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References

1. Lin S, Gao K, Gu S, You L, Qian S, Tang M, et al. Worldwide trends in cervical cancer incidence and mortality, with predictions for the next 15 years. *Cancer*. 2021;**127**(21):4030-9. [PubMed ID: 34368955]. https://doi.org/10.1002/cncr.33795.
2. Luvian-Morales J, Gutierrez-Enriquez SO, Granados-Garcia V, Torres-Poveda K. Risk factors for the development of cervical cancer: analysis of the evidence. *Front Oncol*. 2024;**14**:1378549. [PubMed ID: 38846977]. [PubMed Central ID: PMC11153748]. https://doi.org/10.3389/fonc.2024.1378549.
3. Francoeur AA, Monk BJ, Tewari KS. Treatment advances across the cervical cancer spectrum. *Nat Rev Clin Oncol*. 2025;**22**(3):182-99. [PubMed ID: 39753753]. https://doi.org/10.1038/s41571-024-00977-w.
4. Covens A, Huang HQ, Monk BJ, Kim YB, Kim MH, DiSilvestro P, et al. Evaluation of efficacy and fertility after nonradical surgical therapy (extra fascial hysterectomy or cone biopsy, with pelvic lymphadenectomy) for stage IA1, IA2, and IB1 cervical cancer (GOG-0278). *Gynecol Oncol*. 2025;**195**:59-65. [PubMed ID: 40056831]. [PubMed Central ID: PMC12094068]. https://doi.org/10.1016/j.ygyno.2025.03.005.
5. Palagudi M, Para S, Golla N, Meduri KC, Duvvuri SP, Vityala Y, et al. Adverse Effects of Cancer Treatment in Patients With Cervical Cancer. *Cureus*. 2024;**16**(2). e54106. [PubMed ID: 38487144]. [PubMed Central ID: PMC10938271]. https://doi.org/10.7759/cureus.54106.
6. Tewari KS, Monk BJ. Immunotherapy plus chemoradiotherapy in cervical cancer management. *Lancet*. 2024;**403**(10434):1310-1. [PubMed ID: 38521084]. https://doi.org/10.1016/S0140-6736(24)00468-9.
7. Barras BJ, Ling T, Rivas F. Recent Advances in Chemistry and Antioxidant/Anticancer Biology of Monoterpene and Meroterpenoid Natural Product. *Molecules*. 2024;**29**(1). [PubMed ID: 38202861]. [PubMed Central ID: PMC10780832]. https://doi.org/10.3390/molecules29010279.
8. Suetsugu F, Tadokoro T, Fujita K, Fujihara S, Sasaki K, Omayu E, et al. Antitumor Effects of Epigallocatechin-3-Gallate on Colorectal Cancer: An In Vitro and In Vivo Study. *Anticancer Res*. 2025;**45**(7):2937-47. [PubMed ID: 40578931]. https://doi.org/10.21873/anticanres.17661.
9. Mishra M, Wasnik K, Sharma A, Kumar K, Verma R, Paik P, et al. Epigallocatechin-3-gallate Synergistically Inhibits the Proliferation of Lung Cancer Cells with Gemcitabine by Induction of Apoptosis Mediated by ROS Generation. *ACS Appl Bio Mater*. 2024;**7**(10):6832-46. [PubMed ID: 39333045]. https://doi.org/10.1021/acsabm.4c00958.
10. Wan C, Ouyang J, Li M, Rengasamy KRR, Liu Z. Effects of green tea polyphenol extract and epigallocatechin-3-O-gallate on diabetes mellitus and diabetic complications: Recent advances. *Crit Rev Food Sci Nutr*. 2024;**64**(17):5719-47. [PubMed ID: 36533409]. https://doi.org/10.1080/10408398.2022.2157372.
11. Alam M, Gulzar M, Akhtar MS, Rashid S; Zulfareen; Tanuja, et al. Epigallocatechin-3-gallate therapeutic potential in human diseases: molecular mechanisms and clinical studies. *Mol Biomed*. 2024;**5**(1):73. [PubMed ID: 39725830]. [PubMed Central ID: PMC11671467]. https://doi.org/10.1186/s43556-024-00240-9.
12. Gasmi A, Menzel A, Benahmed AG, Uminska K, Mykhailenko O, Georgiyants V, et al. Anti-cancer Properties of Epigallocatechin-3-gallate (EGCG) and its Signaling Pathways. *Curr Med Chem*. 2025;**32**(35):7724-51. [PubMed ID: 40248930]. https://doi.org/10.2174/0109298673348926250331150429.
13. Wang G, Wang J, Momeni MR. Epigallocatechin-3-gallate and its nanoformulation in cervical cancer therapy: the role of genes, MicroRNA and DNA methylation patterns. *Cancer Cell Int*. 2023;**23**(1):335. [PubMed ID: 38129839]. [PubMed Central ID: PMC10740301]. https://doi.org/10.1186/s12935-023-03161-9.

14. Minnelli C, Cianfruglia L, Laudadio E, Mobbili G, Galeazzi R, Armeni T. Effect of Epigallocatechin-3-Gallate on EGFR Signaling and Migration in Non-Small Cell Lung Cancer. *Int J Mol Sci*. 2021;**22**(21). [PubMed ID: 34769263]. [PubMed Central ID: PMC8583909]. https://doi.org/10.3390/ijms222111833.
15. Chen S, Nishi M, Morine Y, Shimada M, Tokunaga T, Kashihara H, et al. Epigallocatechin-3-gallate hinders metabolic coupling to suppress colorectal cancer malignancy through targeting aerobic glycolysis in cancer-associated fibroblasts. *Int J Oncol*. 2022;**60**(2). [PubMed ID: 35029285]. [PubMed Central ID: PMC8776327]. https://doi.org/10.3892/ijo.2022.5309.
16. Zhang S, Xu H, Zhang L, Qiao Y. Cervical cancer: Epidemiology, risk factors and screening. *Chin J Cancer Res*. 2020;**32**(6):720-8. [PubMed ID: 33446995]. [PubMed Central ID: PMC7797226]. https://doi.org/10.21147/j.issn.1000-9604.2020.06.05.
17. Perkins RB, Wentzensen N, Guido RS, Schiffman M. Cervical Cancer Screening: A Review. *JAMA*. 2023;**330**(6):547-58. [PubMed ID: 37552298]. https://doi.org/10.1001/jama.2023.13174.
18. Capasso L, De Masi L, Sirignano C, Maresca V, Basile A, Nebbioso A, et al. Epigallocatechin Gallate (EGCG): Pharmacological Properties, Biological Activities and Therapeutic Potential. *Molecules*. 2025;**30**(3). [PubMed ID: 39942757]. [PubMed Central ID: PMC11821029]. https://doi.org/10.3390/molecules30030654.
19. Karaman Evren D, Kozgus Guldu O, Tut E, Medine EI. Nanoencapsulation of green tea catechin (−)-Epigallocatechin-3-Gallate (EGCG) in niosomes and assessment of its anticancer activity against lung cancer. *J Drug Deliv Sci Technol*. 2024;**93**. https://doi.org/10.1016/j.jddst.2024.105412.
20. Li X, Hou Y, Han G, Yang Y, Wang S, Lv X, et al. S100A4/NF-kappaB axis mediates the anticancer effect of epigallocatechin-3-gallate in platinum-resistant ovarian cancer. *iScience*. 2024;**27**(2):108885. [PubMed ID: 38313051]. [PubMed Central ID: PMC10835441]. https://doi.org/10.1016/j.isci.2024.108885.
21. Das T, Mondal S, Das S, Das S, Das Saha K. Enhanced anticancer activity of (-)-epigallocatechin-3-gallate (EGCG) encapsulated NPs toward colon cancer cell lines. *Free Radic Res*. 2024;**58**(10):565-82. [PubMed ID: 38810269]. https://doi.org/10.1080/10715762.2024.2360013.
22. Zhang Y, Duan W, Owusu L, Wu D, Xin Y. Epigallocatechin-3-gallate induces the apoptosis of hepatocellular carcinoma LM6 cells but not non-cancerous liver cells. *Int J Mol Med*. 2015;**35**(1):117-24. [PubMed ID: 25370579]. https://doi.org/10.3892/ijmm.2014.1988.
23. Chen L, Ye HL, Zhang G, Yao WM, Chen XZ, Zhang FC, et al. Autophagy inhibition contributes to the synergistic interaction between EGCG and doxorubicin to kill the hepatoma Hep3B cells. *PLoS One*. 2014;**9**(1). e85771. [PubMed ID: 24465696]. [PubMed Central ID: PMC3897495]. https://doi.org/10.1371/journal.pone.0085771.
24. Sovilj D, Kelemen CD, Dvorakova S, Zobalova R, Raabova H, Kriska J, et al. Cell-specific modulation of mitochondrial respiration and metabolism by the pro-apoptotic Bcl-2 family members Bax and Bak. *Apoptosis*. 2024;**29**(3-4):424-38. [PubMed ID: 38001340]. https://doi.org/10.1007/s10495-023-01917-2.
25. Boon NJ, Oliveira RA, Korner PR, Kochavi A, Mertens S, Malka Y, et al. DNA damage induces p53-independent apoptosis through ribosome stalling. *Science*. 2024;**384**(6697):785-92. [PubMed ID: 38753784]. https://doi.org/10.1126/science.adh7950.
26. Mirzayans R. What Is Apoptosis and Why Is It Inhibited by the Most Important Tumor Suppressor (p53)? *Int J Mol Sci*. 2025;**26**(21). [PubMed ID: 41226542]. [PubMed Central ID: PMC12610564]. https://doi.org/10.3390/ijms262110505.
27. Chen J, Ji Z, Wu D, Wei S, Zhu W, Peng G, et al. MYBL2 promotes cell proliferation and inhibits cell apoptosis via PI3K/AKT and BCL2/BAX/Cleaved-caspase-3 signaling pathway in gastric cancer cells. *Sci Rep*. 2025;**15**(1):9148. [PubMed ID: 40097530]. [PubMed Central ID: PMC11914465]. https://doi.org/10.1038/s41598-025-93022-4.
28. Ichisaka Y, Yano S, Nishimura K, Niwa T, Shimizu H. Indoxyl sulfate contributes to colorectal cancer cell proliferation and increased EGFR expression by activating AhR and Akt. *Biomed Res*. 2024;**45**(2):57-66. [PubMed ID: 38556263]. https://doi.org/10.2220/biomedres.45.57.
29. Xu T, Liu K, Zhang Y, Chen Y, Yin D. EGFR and Hippo signaling pathways are involved in organophosphate esters-induced proliferation and migration of triple-negative breast cancer cells. *Environ Sci Pollut Res Int*. 2024;**31**(29):41939-52. [PubMed ID: 38856849]. https://doi.org/10.1007/s11356-024-33872-z.