Available online at www.medicinescience.org

ORIGINAL ARTICLE

Medicine Science International Medical Journal

Medicine Science 2025;14(4):963-8

Antiproliferative and epigenetic effects of tannic acid on MCF-7 human breast cancer cells

Sumeyya Deniz Aybek, Gonca Gulbay, Mucahit Secme

Ordu University, Faculty of Medicine, Department of Medical Biology, Ordu, Türkiye

Received 19 May 2025; Accepted 08 July 2025
Available online 15 September 2025 with doi: 10.5455/medscience.2025.05.128

Abstract

In breast carcinoma, epigenetic modifications, particularly disruption of histone acetylation, have become a significant research focus in recent years for discovering new treatments. Tannic acid (TA) has emerged as one of the promising anti-cancer polyphenolic compounds that suppresses the growth of cancer cells via the suppression of major stages of carcinogenesis. TA is not only a potent inhibitors of the hallmarks of cancer but also it provides pharmacological scaffolds that modulate the epigenetic regulation of gene expression. We investigated in vitro antiproliferative and epigenetic impacts of TA on MCF-7 human breast cancer cells. To our knowledge, there is no preclinical research investigating the epigenetic effect of TA on breast cancer by assessing histone deacetylases (HDACs) expression. The MCF-7 cell viability after TA treatment (12.5-200 µM) for 24-hours was assessed by the MTT assay. To determine the HDACs gene expression changes, total RNA was isolated from MCF-7 cells treated with TA and untreated control cells. The cDNAs were synthesized by Reverse transcription assay and gene expressions were analyzed using qRT-PCR. We found that TA can suppress MCF-7 cell proliferation with a dose-dependent manner as the IC_{50} was 103.7 µM for 24 h. Also, TA treatment led to a marked downregulation of *HDAC1*, *HDAC2*, *HDAC3*, and *HDAC4* expression in MCF-7 cells. This downregulation suggesting that TA may suppress breast cancer cell growth by modulating histone deacetylases activity and potentially inducing epigenetic changes.

Keywords: Breast cancer, histone deacetylases, histone deacetylases inhibitors, tannic acid

Introduction

Breast cancer is the most common malignancy and is the second leading cause of death due to cancer worldwide among females [1]. It is a highly heterogeneous disease in terms of genetics, histology, and prognosis. The cancer heterogeneity is driven by alterations the genomic, transcriptomic, epigenomic, and proteomic profiles of tumor cells. All these molecular alterations influence characteristics of tumor cells such as cell proliferation, metastasis, and apoptosis are pivotal for malignant cancer progression [2,3]. Recently, the epigenetic modifications, particularly acetylation of histone proteins, have become a significant research focus on breast cancer [4,5].

Histone acetylation is a post-translational modification in which an acetyl group is added to the lysine residues of histone. Histone deacetylases (HDACs) and histone acetyltransferases (HATs), two antagonistic enzyme families, modulate histone acetylation [6]. HDACs are responsible for removing of acetyl groups from ε-lysine residues on target proteins, influencing chromatin structure and gene expression. These enzymes can be divided into two families: sirtuins (NAD^+-dependent HDACs) and classical HDACs (Zn^{2+}-dependent HDACs) [7]. Histone deacetylation is a major modification that represses gene expression by a variety of mechanisms. This process increases ionic interactions thereby strengthening interactions between DNA and histone tails and inhibiting access of

CITATION
Aybek SD, Gulbay G, Secme M. Antiproliferative and epigenetic effects of tannic acid on MCF-7 human breast cancer cells. Med Science. 2025;14(4):963-8.

Corresponding Author: Gonca Gulbay, Ordu University, Faculty of Medicine, Department of Medical Biology, Ordu, Türkiye
Email: goncagulbay@odu.edu.tr

DOI: 10.5455/medscience.2025.05.128

transcription complex to promoters. Histone deacetylation also allows to additional regulation via histone methyl-transferases. These post-translational modifications gradually decrease the accessibility of transcription complexes to DNA, leading to enhanced transcriptional silencing [8]. Studies suggest that aberrant expressions of HDACs can affect gene expressions and cellular processes that contribute to carcinogenesis, including apoptosis, proliferation, cell cycle, differentiation, invasion, angiogenesis, and metastasis [9]. Researcher have demonstrated that HDACs may serve as valuable biomarkers for prognosis of breast carcinoma [4,5]. Growing evidence demonstrates that histone deacetylases inhibitors (HDACi) have emerged as potential therapeutic candidates for the treatment of breast cancer due to their ability to regulate expression of tumor suppressor genes by suppressing the activity of HDACs [10,11]. Although clinical use of pan HDACi is considered as a promising therapeutic strategy against breast carcinoma, these agents were associated with unsatisfactory clinical outcomes due to the endurance of serious side effects [1]. Therefore, there is need to discover novel HDACi with an improved therapeutic index, fewer adverse effects, and selective targeting of distinct HDAC isoforms.

Natural compounds have gained significant attention due to their pleiotropic effects across various cancer types, including breast cancer [12,13]. *In vitro* experiments highlight the ability of polyphenolic compounds to modulate epigenetic modification [14]. Curcumin is one of these polyphenol compounds and is reported to inhibit HDACs activity [15]. Quercetin is one of the most studied polyphenol compounds and has been shown to reduce the protein expressions of class I HDACs [16]. However, there are only limited studies to identify the effects of polyphenols on epigenetic modulation.

Tannic acid (TA) is a plant-derived polyphenol that is abundant in plants including nuts, grains, tea, oaks, and fruits [12,13]. TA is considered as an effective flavouring agent to test for cancer therapy, due to its anticarcinogenic actions and limited toxicity [17,18]. It inhibits the growth of tumor cells through the suppression of major stages of carcinogenesis via the modulation of oncological signaling pathways [19]. TA is not only potent inhibitor of the hallmarks of cancer but also provides pharmacological scaffolds that modulate the epigenetic regulation of genes. Previous studies have demonstrated that TA suppressed HAT activity and decreased the expression of DNA methyltransferases [13,20].

Despite many in vitro studies suggesting the antitumoral activity of TA in different malignant cell populations, the mechanisms of action of TA during cancer regression is largely unclear. To our knowledge, there is no research investigating the epigenetic impact of TA on breast cancer by assessing HDACs expression. The main objective of our study is to assess antiproliferative and epigenetic effects of TA on MCF-7 cells. Understanding the effects of TA on HDACs expressions could provide novel perspectives into its therapeutic potential as HDACi in breast carcinoma.

Material and Methods

Cell Culture

Given that this is a cell culture study, ethical approval from an ethics committee is not required. The MCF-7 cells were grown in DMEM high glucose (Gibco, USA) supplemented with 1% penicillin (100 U/mL)/streptomycin (0.1 mg/mL) (Sigma Aldrich, USA) and 10% FBS (HyClone, USA) optimal conditions of 37°C in a CO_2 concentration of 5%. TA was purchased from Sigma-Aldrich (USA), dissolved in dimethyl sulfoxide (Sigma-Aldrich, USA) and subsequently diluted with DMEM to its final concentrations. The final concentration of dimethyl sulfoxide in the culture medium did not exceed 0.01%.

Cell Viability Assay

MTT assay was performed by according to the kit's protocol to determine the antiproliferative effect of TA. The cells were seeded into 96-well plates in media at density of 1.0×10^4 cells/well for 24-hours and then treated with TA (12.5-200 µM) or without. After 24 h, a stock solution of MTT (GoldBio, USA) at a concentration of 5 mg/mL was prepared in PBS and filtered. MTT solution (10 µL/well) was added followed by incubation at 37°C for 3 h, and the media was removed via aspiration. The dimethyl sulfoxide (100 µL/well) was added followed by incubation at 37°C for 15 min. Finally, the colour intensity was measured in a microplate reader at 570 nm. The half maximum inhibitory concentration (IC_{50}) of TA was analysed using non-linear regression with GraphPad Prism. Cell viability of MCF-7 cell was expressed as a percentage, calculated by following formula:

Cell Viability (%)=[(Treatment cell OD_{570} - Blank well OD_{570}) / (Untreated cell OD_{570} - Blank well OD_{570})] ×100%.

qRT-PCR Analysis of Gene Expression

After being treated with 103.7 µM TA for 24-h, MCF-7 cells were rinsed in PBS and harvested with a cell scraper. RNA was isolated by using TRIzol reagent (Hibrigen, Türkiye), according to the kit's protocol. cDNA synthesis was performed using OneScript plus cDNA synthesis kit (Applied Biological Materials, Canada). The reactions were performed with primers specific for HDAC genes (Table 1) in a Rotor Gene 6000 RT-qPCR Thermocycler (Corbett Research, Australia) with qPCR SYBER-Green Master Mix (NucleoGene, Türkiye) and the following protocol: 95°C, 15 min, followed by 40 cycles of 95°C, 15 sec, and 60°C, 1 min. Relative expression levels of *HDAC1*, *HDAC2*, *HDAC3*, and *HDAC4* genes, were calculated using the comparative $2^{-\Delta\Delta Ct}$ method, and ACTB was used as endogenous control.

DOI: 10.5455/medscience.2025.05.128

Table 1. Sequences of primers used for qRT-PCR

Gene symbol	Gene name	Primers
HDAC1	**Histone deacetylase 1**	F: GGTCCAAATGCAGGCGATTCCT R: TCGGAGAACTCTTCCTCACAGG
HDAC2	**Histone deacetylase 2**	F: CTCATGCACCTGGTGTCCAGAT R: GCTATCCGCTTGTCTGATGCTC
HDAC3	**Histone deacetylase 3**	F: GAGTTCTGCTCGCGTTACACAG R: CGTTGACATAGCAGAAGCCAGAG
HDAC4	**Histone deacetylase 4**	F: AGGTGAAGCAGGAGCCCATTGA R: GGTAGTTCCTCAGCTGGTGGAT
ACTB	**Actin beta**	F: CACCATTGGCAATGAGCGGT R: AGGTCTTTGCGGATGTCCAC

F: Forward; R: Reverse

Statistical Analyses

GraphPad Prism 9.4.1 software (GraphPad Software Inc., USA) was employed for statistical analysis of the cell viability experiments. qRT-PCR data can be analyzed using Gene Globe RT² Profiler PCR Data Analysis software (Qiagen). The data represent the mean values±SD and mean values±SEM of three independent experiments performed in triplicate. Kruskal–Wallis test followed by Dunn's post hoc test was used to compare the different experimental groups. For two independent sample comparisons unpaired t-test was performed with differences being considered significant at P values <0.05 (ns P>0.05, *P≤0.05, **P≤0.01, ***P≤0.001, and ****P≤0.0001).

Results

Tannic Acid Inhibits the Proliferation and Viability of MCF-7 Cells

The MCF-7 cell viability after TA treatment (12.5-200 μM) for 24 hours was assessed by the MTT assay. As depicted in Figure 1A, TA dose-dependently reduced MCF-7 cell viability, with an IC_{50} value of 103.7 μM (95% CI: 78.75-144.6 μM) (Figure 1B). After treatment with 200 μM of TA, the viability of MCF-7 cells was significantly decreased (P=0.027).

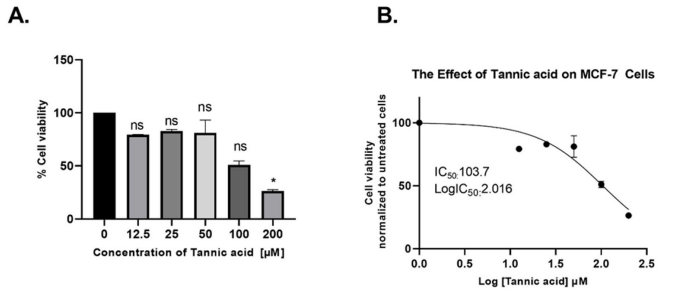

Figure 1. Effect of TA on the proliferation of MCF-7 cells; (**A**) The effect of TA on cell viability and (**B**) Dose-response curve of cell viability; The values are reported as cell viability percentage (%) normalized to untreated MCF-7 cells; The data are presented as mean±S.D. (ns P>0.05, *P≤0.05, **P≤0.01, ***P≤0.001, and ****P≤0.0001)

Tannic Acid Decreases HDAC*s* Expression in MCF-7 Cells

To examine whether HDACs expression levels were altered by TA, MCF-7 cells were treated with IC_{50} dose (103.7 μM) of TA for 24-hours. We found that the treatment of MCF-7 cells with TA significantly reduced mRNA-expression levels of *HDAC1* (17.5-fold; P=0.0011), *HDAC2* (8.4-fold; P=0.024), *HDAC3* (12.8-fold; P=0.004), and *HDAC4* (5.8-fold; P=0.001) compared to those in untreated MCF-7 cells (Figure 2).

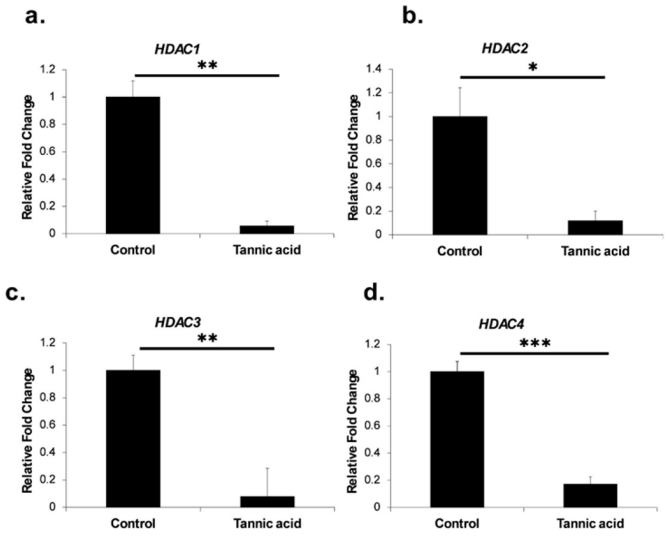

Figure 2. Effect of TA on HDACs gene expression in MCF-7 cells; **a.** HDAC1 **b.** HDAC2 **c.** HDAC3 **d.** HDAC4; The data are presented as mean±SEM (ns P>0.05, *P≤0.05, **P≤0.01, ***P≤0.001, and ****P≤0.0001)

Discussion

Recently, the use of HDACs as therapeutic targets in various types of tumors, especially breast cancer, and their potential clinical value in terms of prognosis have been intensively studied. In a study, a significant correlation was shown between positive hormone receptor (HR-positive) expression and *HDAC1* and *3* protein expression in breast cancer tissues [4]. Similar to this study., Zhang et al. indicated that *HDAC1* mRNA expression was significantly elevated in HR-positive breast cancer patients [21]. In primary tumors, Müller et al. [5] examined a differential positive expression of *HDAC1*, *2* and *3* using immunohistochemical analysis. Protein levels of HDAC2 and *3* were found significantly higher in hormone receptor negative and less differentiated tumors. Conversely, increased level of HDAC1 was observed in HR-positive breast cancer patients. It has been documented that a significant correlation between protein levels of all three isoform and clinicopathological parameters. Expression HDAC2 was also found significantly higher in tumors with positive lymph node metastasis and HER2 overexpression.

Also, HDACi are gaining recognition as potential therapeutic candidates for breast cancer treatment due to their ability to modulate transcription of tumor suppressor genes by suppressing the activity of HDACs [10]. Preclinical studies demonstrated that

DOI: 10.5455/medscience.2025.05.128

HDACi can significantly reduce the proliferation of MCF-7 cells through mechanisms including apoptosis induction, cell cycle arrest, and modulation of gene expressions [11]. Furthermore, preclinical studies have been shown that combining HDACi with chemotherapy drugs can effectively enhances the durability of tumor reduction in treatment of breast carcinoma [22]. Although clinical use of pan HDACi was reported in preclinical studies as a promising therapeutic strategy against breast cancer, these agents were associated with unsatisfactory clinical outcomes due to the endurance of serious side effects [1]. Therefore, there is need to discover novel HDACi with an improved therapeutic index, fewer adverse effects, and selective targeting of distinct HDAC isoforms.

TA is a plant-derived polyphenol that exhibits anticancer effect against different types of cancer including colorectal cancer [23], non-small cell lung cancer (NSCLC) [24], liver cancer [25], and breast cancer [12]. While TA has potent anticancer effects on various cancer cells, it had a little impact on normal healthy cells including human nasal cells [17], human epithelial cells [26], human bronchial epithelial cells [18], and human skin cells [27] which is favorable for anti-cancer therapy. Studies have shown that in NSCLC cells, TA induces intrinsic apoptosis and cell cycle arrest at G0/G1 phase [24] and in prostate cancer cells, it promotes ER stress-mediated apoptosis [28]. Another anticancer mechanism of TA is that it inhibits the major stages of carcinogenesis via the modulation of oncological signaling pathways including TGF-β1/TGF-β1R, VEGF/VEGFR, RAS/RAF/mTOR, JAK/STAT, and CXCL12/CXCR4 axes [19]. Previous in vitro research has also suggested the anti-tumor effect of TA on breast cancer through multiple signaling pathways. Darvin et al. reported TA regulates P38/STAT1/p21 Waf1/Cip1 and EGF-R/Jak2/STAT1/3 pathways and induces G1-arrest and apoptosis via the intrinsic pathway in breast cancer cell lines (BCCLs) [12]. TA was reported to possess the functions of down-regulating FAS expression, inhibiting intracellular FAS activity, in BCCLs, and inducing apoptosis [29]. It also induces upregulation of p53 in breast carcinoma, reduces the cell proliferation of MDA-MB-231 cells, and augments therapeutic efficacy of doxorubicin [30]. In addition, in studies related to breast cancer, it was observed that MCF-7 cells are more sensitive to anti-cancer impacts of TA normal breast epithelial cells, and this compound can induce caspase-mediated apoptosis [26].

Our results showed that TA has notable antiproliferative activity against MCF-7 cells. We found that TA can suppress MCF-7 cell proliferation with a dose-dependent manner as the IC_{50} was 103.7 μM for 24 h. Nie et al. showed that TA reduced the growth of MDA-MB-231 and MCF-7 cell lines [29]. This study reported the concentration and time-dependent manner antiproliferative effects of TA, and IC_{50} values for above cell lines were 2.5 and 4 μM for 24 h, respectively. Hatami et al. found that TA can inhibit cell proliferation in NSCLC cells, and the inhibition concentration were 21.58 and 7.136 μM for the H1299 cells and 23.76 and 10.69 μM for the A549 cells, at 48 and 72 h, respectively [18]. Also, similar to us these studies indicated that the TA cytotoxic effect was mainly dose-dependent. The variation in IC_{50} values between studies may be attributed to differences in experimental conditions such as cell density, exposure duration, and culture environment. Moreover, differences in IC_{50} values are also expected due to the intrinsic biological variability among different cell lines. Therefore, observed variations highlight the necessity of testing anticancer agents in multiple models to better assess their efficacy and selectivity. Zheng et al. also analyzed the antitumoral activity of TA combined with cisplatin in lung cancer cell lines. They reported that this combination treatment suppressed lung cancer cell viability suggesting a synergistic anticancer activity [31].

Polyphenols are abundantly present in fruits and vegetables and are reported to have anti-tumor activity against a variety of cancers, both in vivo and in vitro [32]. Accumulating evidence indicates that the ability of polyphenolic compounds to modulate epigenetic modification including either histone modifications, DNA methylation, or non-coding RNAs [14,33]. By targeting epigenetic enzymes such as HATs, DNA methyltransferases, and HDACs, polyphenols may be an important and innovative treatment strategy, particularly in hormone-related cancers such as breast cancer. In in vitro study related to breast cancer, it was observed that quercetin effectively suppressed activity of p300 HAT in BCCLs [34]. In another study, it was found that combination therapy of pterostilbene and resveratrol significantly down-regulated Sirtuin 1 enzyme in breast cancer cells [35].

Previous studies analyzed effects of TA on modifying the epigenetic regulation of gene expressions. Rashidipour et al. evaluated the epigenetic effects of TA-loaded Chitosan based-nanoparticles in HepG2 cells. They found that these nanoparticles significantly reduced expression of DNA methyltransferases [13]. Chung et al. indicated that TA decreased acetylation of histone H3 protein in an in vitro non-alcoholic fatty liver disease model [20]. To our knowledge, there are no studies investigating the epigenetic impacts of TA on breast cancer by assessing HDACs expression. Our results showed that TA considerably decreased the mRNA expressions of *HDAC1-4* in MCF-7 cells. This finding is in accordance with other studies, suggesting that phenolic compounds may act as HDACi. Alvarez et al. reported that polyphenol quercetin treatment decreases the protein levels of class I HDACs in U937 and HL60 cell lines [16]. Namwan et al. demonstrated that curcumin, a polyphenolic compound, and its derivative CU17 effectively inhibited HDACs activity in A549 cells [15].

HDACs can repress tumor suppressor gene expression and modulate the oncogenic signaling pathways by altering the activity of key regulatory molecules. Inhibition or knockdown of specific HDACs has been consistently associated with cell cycle arrest through modulation of key regulators of the cell cycle progression. For instance, *HDAC1* has been shown to suppress the cyclin-dependent kinase inhibitor p21 in mouse embryonic stem cells thereby promotes cellular proliferation

DOI: 10.5455/medscience.2025.05.128

[36]. In addition to their roles in cell cycle regulation, HDACs have also been shown to regulate apoptosis by modulating expression of pro- and anti-apoptotic proteins. For example, depletion of *HDAC2* has been reported to suppress tumor cell growth and induce apoptosis in human lung cancer through the activation of p53 and Bax and suppression of Bcl2 [37]. These findings collectively suggest that HDACs play pivotal roles in apoptosis and cell cycle progression. We found that TA suppress proliferation and decreased the mRNA expressions of *HDAC1-4* in MCF-7 cells. This results suggesting that TA may suppress breast cancer cell growth by modulating histone deacetylases activity and potentially inducing epigenetic changes.

One of the limitations of our study is that the experiments were performed using only MCF-7 cell line, which may not fully represent the heterogeneity of breast carcinoma. Furthermore, the effects of TA on HDACs protein levels, enzymatic activity, and other post-translational modifications were not explored, limiting our understanding of its full mechanism of action.

Conclusion

Tannic acid exerts anticancer activities in a dose- and time-dependent manner and has been demonstrated to be effective in the treatment of many types of cancer specifically targeting malignant tumors. The purpose of this study was to evaluate the in vitro antiproliferative and epigenetic impacts of TA in MCF-7 cell line. Overall, we observed a significant reduction in the mRNA expressions of HDAC genes upon TA treatment, suggesting that TA may suppress breast cancer cell growth by modulating histone deacetylases activity and potentially inducing epigenetic changes. Future research will focus on validating the effects of TA on HDACs protein expression and enzymatic activity, exploring its binding mechanisms, and testing its efficacy across different breast cell lines.

Conflict of Interests
The authors declare that there is no conflict of interest in the study.

Financial Disclosure
The authors declare that they have received no financial support for the study.

Ethical Approval
Since it is a cell culture study, it does not require ethics committee approval.

Acknowledgments
We would like to thank Dr. Canan Eroglu Gunes (Necmettin Erbakan University) for her contribution in providing the MCF-7 breast cancer cell line used in the present study.

References

1. Mehmood SA, Sahu KK, Sengupta S, et al. Recent advancement of HDAC inhibitors against breast cancer. Med Oncol. 2023;40:201.
2. Guo L, Kong D, Liu J, et al. Breast cancer heterogeneity and its implication in personalized precision therapy. Exp Hematol Oncol. 2023;12:3. Erratum in: Exp Hematol Oncol. 2024;13:7.
3. Lüönd F, Tiede S, Christofori G. Breast cancer as an example of tumour heterogeneity and tumour cell plasticity during malignant progression. Br J Cancer. 2021;125:164-75.
4. Krusche CA, Wülfing P, Kersting C, et al. Histone deacetylase-1 and -3 protein expression in human breast cancer: a tissue microarray analysis. Breast Cancer Res Treat. 2005;90:15-23.
5. Müller BM, Jana L, Kasajima A, et al. Differential expression of histone deacetylases HDAC1, 2 and 3 in human breast cancer - overexpression of HDAC2 and HDAC3 is associated with clinicopathological indicators of disease progression. BMC Cancer. 2013;13:215.
6. Li Y, Seto E. HDACs and HDAC Inhibitors in cancer development and therapy. Cold Spring Harb Perspect Med. 2016;6:a026831.
7. Núñez-Álvarez Y, Suelves M. HDAC11: a multifaceted histone deacetylase with proficient fatty deacylase activity and its roles in physiological processes. FEBS J. 2022;289:2771-92.
8. Gallinari P, Marco SD, Jones P, et al. HDACs, histone deacetylation and gene transcription: from molecular biology to cancer therapeutics. Cell Res. 2007;17:195-211
9. Alseksek RK, Ramadan WS, Saleh E, El-Awady R. The role of HDACs in the response of cancer cells to cellular stress and the potential for therapeutic intervention. Int J Mol Sci. 2022;23:8141.
10. Li G, Tian Y, Zhu WG. The roles of histone deacetylases and their inhibitors in cancer therapy. Front Cell Dev Biol. 2020;8:576946.
11. Yeung A, Bhargava RK, Ahn R, et al. HDAC inhibitor M344 suppresses MCF-7 breast cancer cell proliferation. Biomed Pharmacother. 2012;66:232-6.
12. Darvin P, Joung YH, Kang DY, et al. Tannic acid inhibits EGFR/STAT1/3 and enhances p38/STAT1 signalling axis in breast cancer cells. J Cell Mol Med. 2017;21:720-34.
13. Rashidipour M, Abbaszadeh S, Birjandi M, et al. Antimicrobial activity and cytotoxic and epigenetic effects of tannic acid-loaded chitosan nanoparticles. Sci Rep. 2024;14:30405.
14. Kiss AK, Granica S, Stolarczyk M, Melzig MF. Epigenetic modulation of mechanisms involved in inflammation: influence of selected polyphenolic substances on histone acetylation state. Food Chem. 2012;131:1015-20.
15. Namwan N, Senawong G, Phaosiri C, et al. HDAC inhibitory and anti-cancer activities of curcumin and curcumin derivative CU17 against human lung cancer A549 cells. Molecules. 2022;27:4014.
16. Alvarez MC, Maso V, Torello CO, et al. The polyphenol quercetin induces cell death in leukemia by targeting epigenetic regulators of pro-apoptotic genes. Clin Epigenetics. 2018;10:139.
17. Alqunaee M, Bayar Muluk N, Turgut Cosan D, Cingi C. Is tannic acid a promising option in local treatment of nasal diseases?. Eur Rev Med Pharmacol Sci. 2023;27:76-82.
18. Hatami E, Nagesh PKB, Sikander M, et al. Tannic acid exhibits antiangiogenesis activity in nonsmall-cell lung cancer cells. ACS Omega. 2022;7:23939-49.
19. Youness RA, Kamel R, Elkasabgy NA, et al. Recent advances in tannic acid (gallotannin) anticancer activities and drug delivery systems for efficacy improvement; a comprehensive review. Molecules. 2021;26:1486.
20. Chung MY, Song JH, Lee J, et al. Tannic acid, a novel histone acetyltransferase inhibitor, prevents non-alcoholic fatty liver disease both in vivo and in vitro model. Mol Metab. 2019;19:34-48.
21. Zhang Z, Yamashita H, Toyama T, et al. Quantitation of HDAC1 mRNA expression in invasive carcinoma of the breast. Breast Cancer Res Treat. 2005;94:11-6.
22. Guerriero JL, Sotayo A, Ponichtera HE, et al. Class IIa HDAC inhibition reduces breast tumours and metastases through anti-tumour macrophages. Nature. 2017;543:428-32.

DOI: 10.5455/medscience.2025.05.128

23. Nejad FS, Karami H, Darvish M. Triggering of endoplasmic reticulum stress by tannic acid inhibits the proliferation and migration of colorectal cancer cells. Asian Pac J Cancer Prev. 2023;24:2705-11.

24. Sp N, Kang DY, Kim DH, et al. Tannic acid inhibits non-small cell lung cancer (NSCLC) stemness by inducing G0/G1 cell cycle arrest and intrinsic apoptosis. Anticancer Res. 2020;40:3209-20.

25. Geng N, Zheng X, Wu M, et al. Tannic acid synergistically enhances the anticancer efficacy of cisplatin on liver cancer cells through mitochondria-mediated apoptosis. Oncol Rep. 2019;42:2108-16.

26. Ngobili TA, Shah H, Park JP, et al. Remodeling of tannic acid crosslinked collagen type I induces apoptosis in ER+ breast cancer cells. Anticancer Res. 2015;35:1285-90.

27. Aguilera JR, Venegas V, Oliva JM, et al. Targeted multifunctional tannic acid nanoparticles. RSC Adv. 2016;6:7279-87.

28. Nagesh PKB, Hatami E, Chowdhury P, et al. Tannic acid induces endoplasmic reticulum stress-mediated apoptosis in prostate cancer. Cancers. 2018;10:68.

29. Nie F, Liang Y, Jiang B, et al. Apoptotic effect of tannic acid on fatty acid synthase over-expressed human breast cancer cells. Tumor Biol. 2016;37:2137-43.

30. Tikoo K, Sane MS, Gupta C. Tannic acid ameliorates doxorubicin-induced cardiotoxicity and potentiates its anti-cancer activity: potential role of tannins in cancer chemotherapy. Toxicol Appl Pharmacol. 2011;251:191-200.

31. Zheng X, Yang L, Zhai W, et al. Synergistic anticancer activity of cisplatin combined with tannic acid enhances apoptosis in lung cancer through the PERK-ATF4 pathway. Eur J Med Res. 2023;28:462.

32. Shabbir U, Rubab M, Daliri EBM, et al. Curcumin, quercetin, catechins and metabolic diseases: the role of gut microbiota. Nutrients. 2021;13:206.

33. Číž M, Dvořáková A, Skočková V, Kubala L. The role of dietary phenolic compounds in epigenetic modulation involved in inflammatory processes. Antioxidants (Basel). 2020;9:691.

34. Xiao X, Shi D, Liu L, et al. Quercetin suppresses cyclooxygenase-2 expression and angiogenesis through inactivation of P300 signaling. PLoS One. 2011;6:e22934.

35. Kala R, Shah HN, Martin SL, Tollefsbol TO. Epigenetic-based combinatorial resveratrol and pterostilbene alters DNA damage response by affecting SIRT1 and DNMT enzyme expression, including SIRT1-dependent γ-H2AX and telomerase regulation in triple-negative breast cancer. BMC Cancer. 2015;15:672.

36. Zupkovitz G, Grausenburger R, Brunmeir R, et al. The cyclin-dependent kinase inhibitor p21 is a crucial target for histone deacetylase 1 as a regulator of cellular proliferation. Mol Cell Biol. 2010;30:1171-81.

37. Jung KH, Noh JH, Kim JK, et al. HDAC2 overexpression confers oncogenic potential to human lung cancer cells by deregulating expression of apoptosis and cell cycle proteins. J Cell Biochem. 2012;113:2167-77.