Eurasian Journal of Molecular and Biochemical Sciences

Unveiling the Dual Role of Gastrodin: Cytotoxic and Antimetastatic Effects in Triple Negative Breast Cancer Cells and Safety in Mesenchymal Stem Cells

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Cite: *Keskin S.U, Sezgin A, Kalender S.M, Bülbül M.V, Unveiling the Dual Role of Gastrodin: Cytotoxic and Antimetastatic Effects in Triple Negative Breast Cancer Cells and Safety in Mesenchymal Stem Cells. Eurasian Mol Biochem Sci 2025;4(2): 89-98*

Received: 29 August 2025, Accepted: 3 September 2025 *DOI: 10.5281/zenodo.17786613*

Abstract

Triple-negative breast cancer (TNBC) represents an aggressive and therapeutically challenging subtype of breast carcinoma, characterized by the absence of estrogen receptor, progesterone receptor, and HER2 expression. Given its propensity for metastasis and limited treatment options, novel therapeutic candidates are urgently needed. Gastrodin, a bioactive compound derived from Gastrodia elata, has demonstrated diverse pharmacological properties, including antioxidant, anti-inflammatory, and anticancer activities. This study aimed to investigate the antiproliferative and antimigratory effects of gastrodin on the MDA-MB-231 TNBC cell line and evaluate its cytotoxicity on non-malignant adipose-derived mesenchymal stem cells (ADMSCs) to assess selectivity. Cell viability was determined using the MTT assay across a concentration range of 5–1000 µM, and wound healing assays were employed to assess migratory behavior. Results indicated a dose-dependent reduction in MDA-MB-231 cell viability, with an IC_{50} of 587.6 µM, while ADMSCs exhibited minimal cytotoxicity at 100 µM, suggesting a favorable safety profile. Furthermore, treatment with 100 µM gastrodin significantly inhibited cell migration compared with untreated controls. These findings underscore the potential of gastrodin as a candidate for TNBC therapy, particularly given its selective cytotoxicity toward malignant cells and its ability to suppress migration, a key step in metastasis. Collectively, this study contributes to the growing evidence supporting natural compounds as promising alternatives for combating aggressive breast cancer subtypes.

Keywords: Breast Neoplasms, Metastasis, TNBC, Gastrodin, Selective cytotoxicity

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Introduction

Breast cancer, the most commonly diagnosed malignancy in women, is characterized by significant molecular heterogeneity (1). Based on the 2023 Cancer Statistics reported by the American Cancer Society, the incidence of breast cancer (BC) has continued to rise, representing approximately 31% of all female malignancies and ranking first among the ten most frequently diagnosed cancers in women (2). Triple-negative breast cancer (TNBC), a biologically aggressive subtype of breast cancer, constitutes approximately 15–20% of all cases and is defined by the lack of estrogen receptor (ER), progesterone receptor (PgR), and human epidermal growth factor receptor 2 (HER2) expression, as assessed through immunohistochemical (IHC) analysis (3) . As a distinct clinical and molecular subtype of BC, TNBC is strongly linked to aggressive clinical progression; nearly 45% of patients experience distant metastases, including to the brain, and the median overall survival is markedly reduced (4).

Metastasis is an organ-specific, multistep process, initiated by the escape of malignant cells from the primary tumor and culminating in the colonization of distant sites with secondary tumor formation (5). The complexity of this sequential cascade significantly contributes to the challenges in achieving effective cancer therapy. This complexity also underlies the limited success in the development of therapeutic agents, often referred to as migrastatics, designed to efficiently inhibit tumor metastasis. To date, numerous metastasis-promoting factors have been identified (6). However, the development of agents capable of targeting the entire metastatic process remains unfeasible, thereby driving continued research efforts in this field.

Gastrodin (4-hydroxybenzyl alcohol-4-O-β-D-glucopyranoside) represents the primary bioactive constituent and serves as a key quality control marker of the traditional Chinese herb Gastrodia elata Blume(7, 8). Gastrodin, with a chemical formula of $C_{13}H_{18}O_7$ and a molecular weight of 286.278 Da, is highly soluble in methanol, ethanol, and water, but remains insoluble in chloroform and ether. It exhibits considerable stability in aqueous, methanolic, ethanolic, and phosphate-buffered saline (PBS) solutions. Additionally, its equilibrium solubility in aqueous media decreases with increasing pH, whereas in organic solvents, solubility declines as solvent polarity decreases (9).

Previous studies have demonstrated that gastrodin exhibits a broad spectrum of pharmacological activities, including anti-inflammatory, antipsychotic, antifibrotic, antioxidant, antiepileptic, anticonvulsant, and antitumor effects (10). A review of studies investigating the anticancer properties of gastrodin has demonstrated that gastrodin (20–30 μM) can suppress the proliferation of DBTRG-05MG human glioblastoma cells by inducing cell cycle arrest at the G2/M phase, enhancing reactive oxygen species (ROS) and Bax expression, and activating caspase-9 and caspase-3, thereby triggering the mitochondrial apoptotic pathway (11). Furthermore, gastrodin exerts anticancer effects by modulating immune responses. In a murine tumor model implanted with H22 hepatoma cells, gastrodin (15–150 mg/kg) enhanced the binding of the NF-κB p65 subunit to the promoter regions of genes encoding IL-2 and Bcl-2 in $CD4^+$ T cells (12). Moreover, gastrodin administration (0.6 mg/mouse) promoted the activation of dendritic cells, macrophages, $CD4^+$ and $CD8^+$ T cells, while inducing upregulation of co-stimulatory molecules (CD80, CD86), major histocompatibility complexes I and II (MHCI, MHCII), and cytokines including IL-2, IFN-γ, perforin, TNF-α, and IFN-α. These immunomodulatory effects were associated with enhanced survival in melanoma-bearing mice and

significant suppression of tumor progression (13). TNBC lacks targeted therapies and demonstrates intrinsic resistance to standard chemotherapeutic regimens, highlighting the urgent need for alternative strategies. Emerging evidence indicates that signaling pathways modulated by gastrodin, including PI3K/AKT, Rho GTPase, and Wnt/β-catenin, play pivotal roles in TNBC biology by regulating processes such as epithelial–mesenchymal transition (EMT), invasion, and metastasis. Thus, investigating gastrodin in TNBC is scientifically justified based on its ability to interfere with molecular mechanisms that drive the aggressive and metastatic phenotype of this cancer subtype (14-16).

The development of anticancer agents necessitates the identification of compounds that selectively target malignant cells while exerting minimal cytotoxic effects on normal, healthy cells. Consequently, incorporating both tumor-derived and non-tumorigenic cell lines in in vitro experiments is essential for accurately assessing the selective toxicity profile of candidate agents (17). This strategy enhances the reliability of preclinical evaluations and facilitates the identification of promising candidates for advancement into clinical trials (18). In this study, rat-derived adipose-derived mesenchymal stem cells (AD-MSCs) were employed as a representative non-malignant cell type to assess the safety profile of gastrodin. Rat AD-MSCs have been widely used in clinical and preclinical studies across different species due to their structural and functional similarities to human MSCs, especially in terms of differentiation potential, surface marker expression and immunomodulatory properties (19). Furthermore, these cells provide an ethically acceptable and cost-effective alternative for initial cytotoxicity screening prior to the use of human-derived MSCs, ensuring compliance with the principles of the 3Rs (Replacement, Reduction, and Refinement) in preclinical research.

This study seeks to expand the existing evidence base supporting gastrodin as a potential therapeutic agent for triple-negative breast cancer (TNBC), one of the most aggressive and treatment-refractory breast cancer subtypes. Furthermore, to evaluate its safety profile, the effects of gastrodin on adipose-derived mesenchymal stem cells (ADMSCs) were examined to assess its impact on non-malignant cells. Through a systematic in vitro approach, the antiproliferative and antimigratory properties of gastrodin were comprehensively characterized, providing valuable insights into its potential as a selective anticancer agent.

Material and Method

Cell Cultures: Rat Adipose-derived mesenchymal stem cells (ADMSCs) were obtained from the Kocaeli University Stem Cell and Gene Therapies Research and Application Center in cryopreserved vials containing 1×10^6 cells. Cell isolation and characterization were performed by the same facility. For culture, low-glucose DMEM (11885084, Gibco) supplemented with 10% fetal bovine serum (F7524, Sigma-Aldrich), 2% L-glutamine (G6392, Sigma-Aldrich), and 1% antibiotic-antimycotic solution (A5955, Sigma-Aldrich) was used. The human triple-negative breast cancer cell line MDA-MB-231 was purchased from ATCC (catalog number HTB-26) in frozen form. These cells were maintained in DMEM/F12 medium (Gibco 31330038) supplemented with 10% fetal bovine serum (ATCC 30-2020) and 1% antibiotic-antimycotic solution (Gibco 15240062). The cryovials were thawed by gentle swirling in a 37°C water bath for approximately one minute, disinfected with 70% ethanol, and all subsequent steps were performed under aseptic conditions. The cell suspension was transferred into a centrifuge tube containing 9 mL of complete medium and centrifuged at 1500 rpm for 5 minutes. Following removal of the supernatant, the pellet was resuspended in 1 mL of complete medium and transferred to a T75

culture flask (Corning #430641) containing 11 mL of complete medium. Cultures were incubated at 37°C in a humidified atmosphere of 95% humidity, 5% CO_2, and 5% O_2 until reaching approximately 80% confluency. Cells were then harvested by trypsinization: the medium was aspirated, cells were rinsed with sterile PBS, and 2 mL of Trypsin/EDTA solution (ATCC 30-2101) was added. After a 5-minute incubation, detached cells were collected in complete medium and centrifuged at 1500 rpm for 3 minutes. The resulting pellet was resuspended in 5 mL of fresh culture medium, and cell counts were determined using a Scepter™ 2.0 Handheld Automated Cell Counter (Merck, C85360).

MTT Cell Viability Assay: The antiproliferative activity of gastrodin on MDA-MB-231 cells and rat adipose-derived mesenchymal stem cells (Rat-ADMSCs) was evaluated using a colorimetric MTT assay [3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide]. Gastrodin was obtained from SigmaAldrich under catalog number SMB00313. Cells were seeded into 96-well plates at a density of 1×10^4 cells per well and incubated for 24 hours to allow adhesion and initial growth. Once approximately 70% confluence was achieved, the culture medium was replaced with complete medium containing gastrodin at concentrations of 5, 25, 50, 100, 250, 500, and 1000 µM. The group that received no gastrodin treatment was designated as the negative control, whereas the group treated with a 1% Triton X solution served as the positive control. Cells were then incubated under standard conditions for an additional 24 hours. Following exposure, the gastrodin-containing medium was removed, and MTT solution was added to each well at a ratio of 1:20 (MTT:total volume), followed by incubation for 3 hours at 37°C in a humidified atmosphere with 5% CO_2. Afterward, the MTT solution was aspirated, and a solubilization mixture of culture medium and DMSO (1:1, v/v) was added. The plates were incubated in the dark on an orbital shaker for 1 hour to ensure complete dissolution of formazan crystals. Absorbance was measured at 570 nm using a microplate spectrophotometer. The half-maximal inhibitory concentration (IC_{50}) was calculated, and dose–response curves and statistical analyses were performed using GraphPad Prism version 9.1 (20). Additionally, morphological changes following 24-hour exposure to the IC_{50} concentration of gastrodin were documented using a Carl Zeiss™ Axio Vert.A1 inverted microscope.

Wound Healing Migration Assay: A wound healing and migration assay was performed using a Culture-Insert 2 Well in a µ-Dish 35 mm (ibidi, Cat. No. 80206). A total of 3×10^5 cells were seeded in 70 µL of medium per well and incubated at 37°C in a humidified atmosphere containing 5% CO_2 for 24 hours to allow proper cell attachment. Following incubation, the Culture-Insert 2 Well was carefully removed using sterile tweezers. Subsequently, 2 mL of medium supplemented with 100 µM gastrodin—previously determined by MTT assays to be non-toxic to ADMSCs while exerting antiproliferative effects on MDA-MB-231 cells—was added to the MDA-MB-231 culture. Untreated MDA-MB-231 cells served as the control group. Images were captured at 0 and 24 hours, and the number of cells migrating into the wound area was quantified and analyzed using ImageJ software (21).

Statistical Analysis: All statistical analyses were performed using GraphPad Prism version 8.0.0, employing the Mann–Whitney U test and one-way ANOVA with multiple comparison procedures. Statistical significance was defined as follows: non-significant ($P > 0.05$), * ($P \leq 0.05$), ** ($P \leq 0.01$), *** ($P \leq 0.001$), and **** ($P \leq 0.0001$).

Result

Specific doses of Gastrodin reduce MDA-MB-231 cell viability without affecting MSCs

The half-maximal inhibitory concentration (IC_{50}) of gastrodin, defined as the concentration reducing cell proliferation by 50%, was calculated as 269.2 µM in rat adipose-derived mesenchymal stem cells (AD-MSCs) (Figure 1).

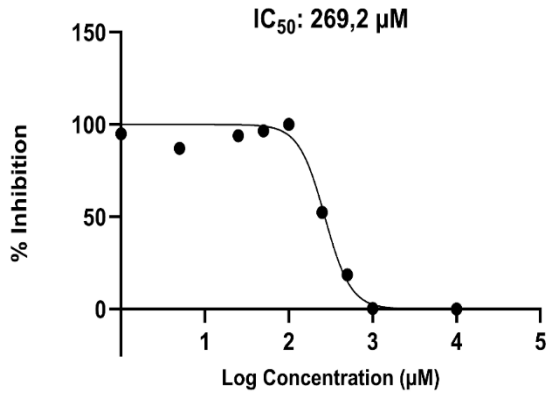

Figure 1. Graphical representation of the viability curve of rat adipose-derived mesenchymal stem cells (AD-MSCs) in response to gastrodin treatmen

Analysis of cell viability across different concentrations revealed a statistically significant decrease at 5 µM compared with the untreated negative control ($P \leq 0.0001$). Conversely, no significant difference was observed between the 25 µM and 50 µM groups and the control. Interestingly, treatment with 100 µM resulted in a significant increase in cell proliferation ($P \leq 0.0001$) relative to the control. At higher concentrations (250 µM, 500 µM, and 1000 µM), a pronounced reduction in cell viability was noted, indicating a strong cytotoxic effect ($P \leq 0.0001$) compared with the negative control (Figures 2 and Table 1).

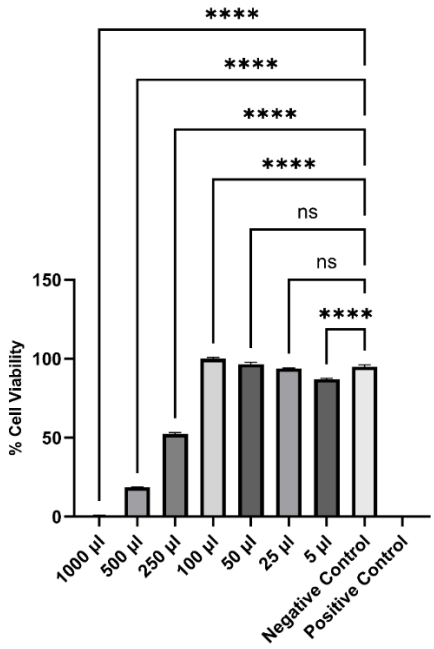

Figure 2. Percentage cell viability of rat adipose-derived mesenchymal stem cells (AD-MSCs) treated with gastrodin (ns: $P > 0.05$, *: $P \leq 0.05$, **: $P \leq 0.01$, ***: $P \leq 0.001$, ****: $P \leq 0.0001$).

Table 1. Percentage cell viability levels and standard error of the mean (SEM) of rat adipose-derived mesenchymal stem cells (AD-MSCs) treated with gastrodin.

Doses (µM)	Cell Viability	SEM
5	87	±0.26
25	93.8	±0.19
50	96.5	±0.72
100	100	±0.45
250	52.3	±0.56
500	18.5	±0.06
1000	8.3	±0.34
Negative Control	94.9	±0.69
Positive Control	0	±0.06

The half-maximal inhibitory concentration (IC_{50}) of gastrodin, defined as the concentration required to reduce cell proliferation by 50%, was determined to be 587.6 µM in MDA-MB-231 cells (Figure 3). A dose-dependent and statistically significant decrease in cell viability ($P \leq 0.0001$) was observed across the seven tested concentrations of gastrodin compared with the untreated negative control group (Figure 4). Furthermore, a noticeable reduction in cell confluency was observed after 24 hours of exposure to 500 µM and 1000 µM concentrations of gastrodin (Figure 5). To evaluate the effects of gastrodin on the migratory potential of MDA-MB-231 cells, wound-healing assays were conducted. In the group treated with 100 µM gastrodin, no significant change (ns) was detected in the number of cells migrating into the wound area between 0 and 24 hours (Figure 6B). In contrast, a significant increase ($P \leq 0.05$) in the number of migrating cells was observed in the control group during the same period (Figure 6B). Moreover, when the number of migrating cells in the treated group was compared with that of the control group, a significantly higher migration rate ($P \leq 0.001$) was observed in the control cells (Figure 6C).

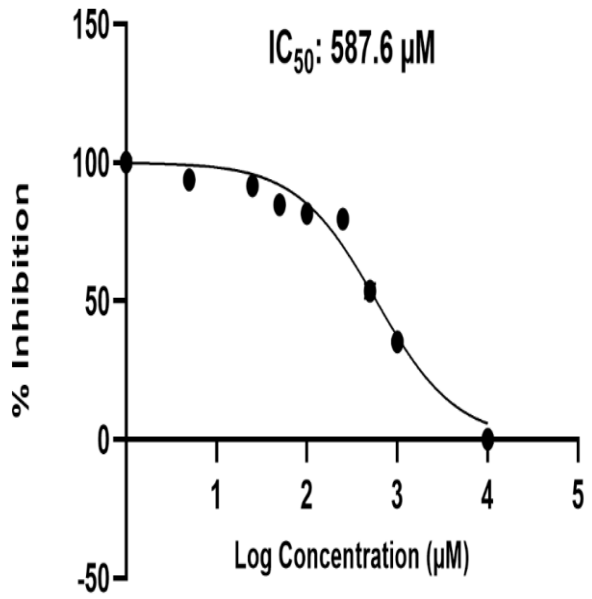

Figure 3. Graphical representation of the viability curve of MDA-MB-231 cells in response to gastrodin treatment.

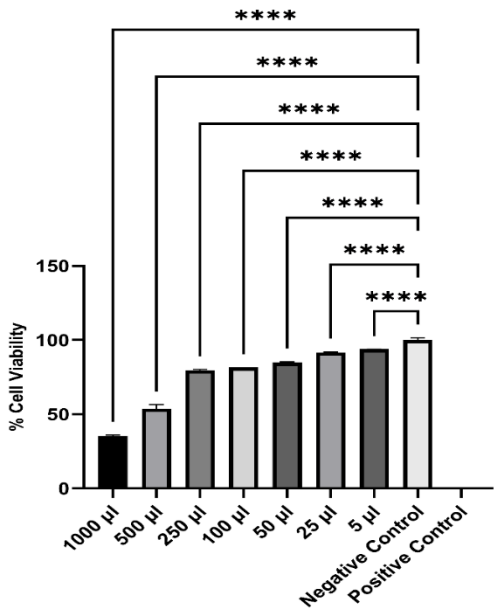

Figure 4. Percentage cell viability of MDA-MB-231cells treated with gastrodin (ns: $P > 0.05$, *: $P \leq 0.05$, **: $P \leq 0.01$, ***: $P \leq 0.001$, ****: $P \leq 0.0001$)

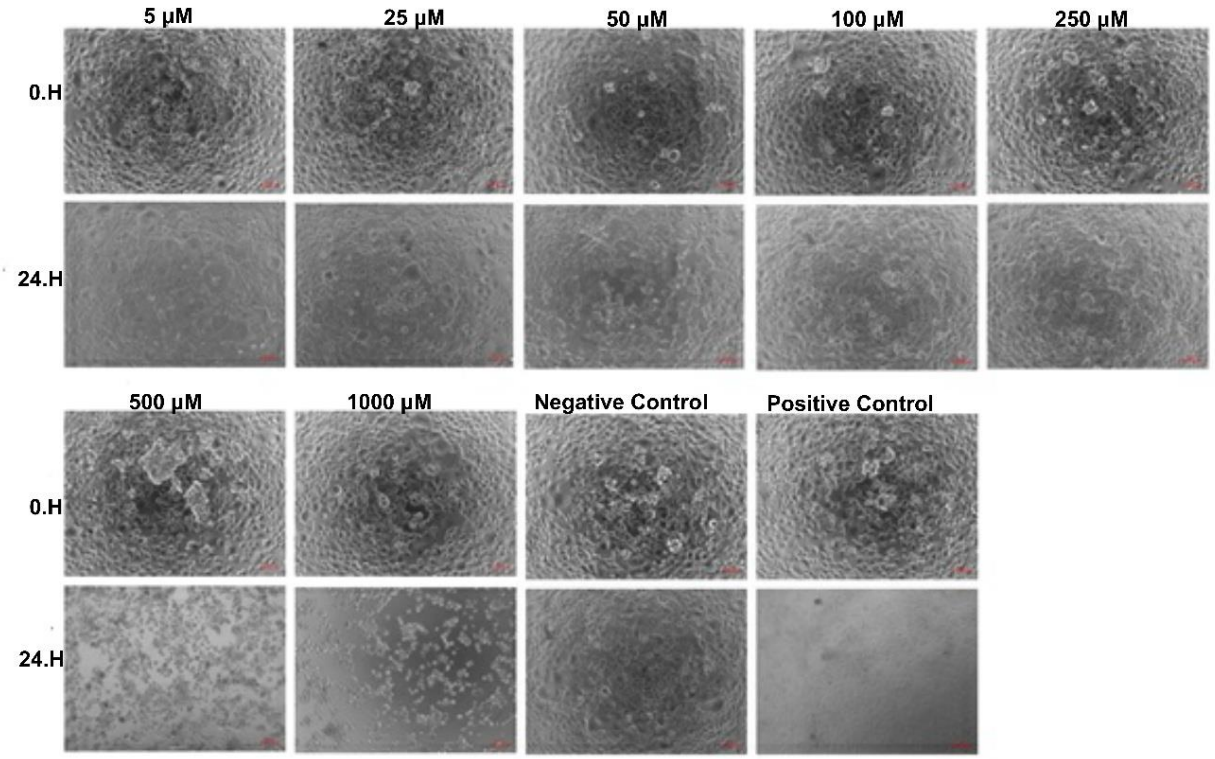

Figure 5. Alterations in the confluency and proliferation profile of MDA-MB-231 cells after 24-hour exposure to different concentrations of gastrodin.

Gastrodin exhibits antimigratory effects on MDA-MB-231 cells

The half-maximal inhibitory concentration (IC_{50}) of gastrodin, defined as the concentration required to reduce cell proliferation by 50%, was determined to be 587.6 µM in MDA-MB-231 cells (Figure 3). A dose-dependent and statistically significant decrease in cell viability ($P \leq 0.0001$) was observed across the seven tested concentrations of gastrodin compared with the untreated negative control group (Figure 4). Furthermore, a noticeable reduction in cell confluency was observed after 24 hours of exposure to 500 µM and 1000 µM concentrations of gastrodin (Figure 5). To evaluate the effects of gastrodin on the migratory potential of MDA-MB-231 cells, wound-healing assays were conducted. In the group treated with 100 µM gastrodin, no significant change (ns) was detected in the number of cells migrating into the wound area between 0 and 24 hours (Figure 6B). In contrast, a significant increase ($P \leq 0.05$) in the number of migrating cells was observed in the control group during the same period (Figure 6B). Moreover, when the number of migrating cells in the treated group was compared with that of the control group, a significantly higher migration rate ($P \leq 0.001$) was observed in the control cells (Figure 6C).

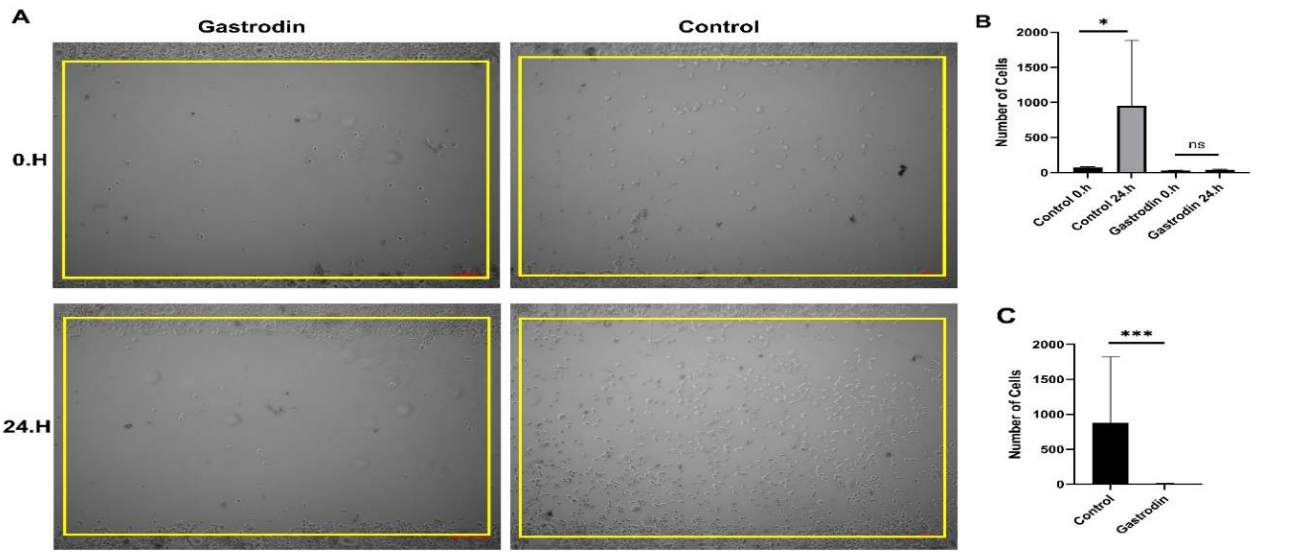

Figure 6. A) Microscopic visualization of migration patterns in MDA-MB-231 cells after 24-hour treatment with 100 µM gastrodin, B) Graph illustrating the number of migrated cells in the experimental and control groups at 24 hours, C) Quantitative comparison of the number of migrated cells in the control group versus the group treated with gastrodin. (ns: $P > 0.05$, *: $P \leq 0.05$, ***: $P \leq 0.001$).

Discussion

This study provides insights into the anticancer potential of gastrodin in triple-negative breast cancer (TNBC), a highly aggressive and treatment-resistant subtype of breast cancer. Our findings demonstrated that gastrodin induced a dose-dependent reduction in cell viability in MDA-MB-231 cells. A previous study reported that gastrodin exerted cytotoxic effects in glioblastoma cells within the 20–30 µM range, while exhibiting no cytotoxicity in normal astrocyte cells (11). In our study, the IC_{50} of gastrodin in MDA-MB-231 cells was determined to be 587.6 µM. This discrepancy may be attributed to the aggressive profile of MDA-MB-231 cells as well as differences in the source of the gastrodin agent used. The rat AD-MSC model has been extensively utilized in toxicology and regenerative medicine research, providing a reliable platform for preclinical evaluation (22).Consistent with previous findings, gastrodin at low, non-toxic concentrations (100 µM) did not induce significant cytotoxicity in healthy rat adipose-derived mesenchymal stem cells (ADMSCs). This selective cytotoxicity profile positions gastrodin as a promising candidate for therapeutic strategies capable of targeting malignant cells while sparing normal cells. The reduced cell density and morphological alterations observed at higher concentrations further support its cytotoxic effects on TNBC cells. Importantly, the absence of significant viability loss in ADMSCs at 100 µM indicates a favorable safety margin for preclinical evaluation. In addition to its cytotoxic effects, gastrodin demonstrated notable anti-migratory properties. In wound healing assays, treatment with 100 µM gastrodin significantly suppressed cell migration in MDA-MB-231 cells over 24 hours, whereas the control group exhibited a pronounced increase in migratory activity.

Gastrodin stimulates the PI3K/AKT signaling pathway, resulting in anti-inflammatory, anti-apoptotic, and antioxidant responses in microglial and endothelial cells. This pathway activation also enhances the expression of Sirt3 and miR-21, facilitating cell survival, motility, and angiogenic processes—key mechanisms implicated in tumor development and progression (23-25). Gastrodin mitigates ketamine-induced disturbances in Rho signaling by modulating

proteins essential for cytoskeletal organization and cell migration, including RhoGDI1, RhoA, ROCK1, MLC2, PFN1, and CFL1. These effects were observed in B35 and C6 cell lines, which, although not TNBC cells, exhibit migratory and cytoskeletal characteristics relevant to cancer metastasis (26). A recent study also demonstrated that gastrodin suppresses prostate cancer cell proliferation through modulation of the canonical Wnt/β-catenin signaling pathway (27). Although previous studies have not directly investigated the impact of gastrodin on antimigratory and antiproliferative signaling in TNBC cells, indirect evidence suggests that gastrodin-regulated pathways—including Rho, PI3K/AKT, Nrf2/HO-1, and TGF-β/Smad—play critical roles in TNBC biology, particularly in key processes such as cell migration, invasion, and therapeutic resistance.

In conclusion, this study demonstrates that gastrodin exerts selective antiproliferative and anti-migratory effects in TNBC cells, while exhibiting limited cytotoxicity in non-malignant ADMSCs at low concentrations. However, several limitations should be acknowledged. First, the study relies solely on in vitro assays, which cannot fully recapitulate the complex in vivo tumor microenvironment, including interactions with the extracellular matrix, stromal cells, and the immune system. Another limitation is the relatively high IC_{50} of gastrodin observed in MDA-MB-231 cells, which may exceed physiologically achievable systemic concentrations. Gastrodin can potentially be administered using nanocarrier-based systems, targeted delivery strategies, or combination therapy approaches to increase bioavailability and reduce the required effective dose. Additionally, several phytochemicals with high in vitro IC_{50} values have demonstrated significant antitumor activity when optimized through advanced delivery systems (28).

Future research should focus on a more detailed characterization of the molecular pathways affected by gastrodin in TNBC cells. In particular, signaling pathways associated with epithelial–mesenchymal transition (EMT), oxidative stress regulation, and apoptosis should be investigated, and key molecular targets mediating these effects should be identified through transcriptomic and proteomic analyses. Validation of these findings in three-dimensional cell culture models and in vivo animal studies will be critical for translational applications. Taken together, our results suggest that, in light of gastrodin's previously reported safety profile and multifaceted biological activities, it represents a promising candidate for TNBC therapy.

Author Contributions Conceptualization: SUK, AS, SMK, MVB. Formal Analysis: SUK, AS, SMK. Investigation: SUK, AS, SMK, MVB. Methodology: SUK, AS, SMK, MVB. Project Administration: SMK, MVB. Writing – Original Draft: SUK, AS, SMK, MVB. Writing – Review & Editing: SMK, MVB.

Declaration of Interest: The author declares that there is no conflict of interest regarding the publication of this paper.

Funding: This study was supported by TUBITAK 2209-A with project numbers 1919B012315576 and 1919B012314525.

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References

1. Sadri F, fatemeh Hosseini S, Rezaei Z, Fereidouni M. Hippo-YAP/TAZ signaling in breast cancer: reciprocal regulation of microRNAs and implications in precision medicine. Genes & Diseases. 2024;11(2):760–71.
2. Siegel RL, Miller KD, Wagle NS, Jemal A. Cancer statistics, 2023. CA: a cancer journal for clinicians. 2023;73(1).
3. Dent R, Trudeau M, Pritchard KI, Hanna WM, Kahn HK, Sawka CA, et al. Triple-negative breast cancer: clinical features and patterns of recurrence. Clinical cancer research. 2007;13(15):4429–34.
4. Schmid P, Adams S, Rugo HS, Schneeweiss A, Barrios CH, Iwata H, et al. Atezolizumab and nab-paclitaxel in advanced triple-negative breast cancer. New England journal of medicine. 2018;379(22):2108–21.
5. Paul CD, Mistriotis P, Konstantopoulos K. Cancer cell motility: lessons from migration in confined spaces. Nature reviews cancer. 2017;17(2):131–40.
6. Majidpoor J, Mortezaee K. Steps in metastasis: an updated review. Medical Oncology. 2021;38(1):3.
7. Taguchi H, Yosioka I, Yamasaki K, KIM I. Studies on the constituents of Gastrodia elata Blume. Chemical and Pharmaceutical Bulletin. 1981;29(1):55–62.
8. Li Y, Zhang Y, Zhang Z, Hu Y, Cui X, Xiong Y. Quality evaluation of gastrodia elata tubers based on HPLC fingerprint analyses and quantitative analysis of multi-components by single marker. Molecules. 2019;24(8):1521.
9. Dai Y, Ban W, Yang Z. Gastrodin, a promising natural small molecule for the treatment of central nervous system disorders, and its recent progress in synthesis, pharmacology and pharmacokinetics. International journal of molecular sciences. 2024;25(17):9540.
10. El Menyiy N, Elouafy Y, Moubachir R, Abdnim R, Benali T, Taha D, et al. Chemistry, biological activities, and pharmacological properties of gastrodin: Mechanism insights. Chemistry & Biodiversity. 2024;21(6):e202400402.
11. Liang W-Z, Jan C-R, Hsu S-S. Cytotoxic effects of gastrodin extracted from the rhizome of Gastrodia elata Blume in glioblastoma cells, but not in normal astrocytes, via the induction of oxidative stress-associated apoptosis that involved cell cycle arrest and p53 activation. Food and Chemical Toxicology. 2017;107:280–92.
12. Shu G, Yang T, Wang C, Su H, Xiang M. Gastrodin stimulates anticancer immune response and represses transplanted H22 hepatic ascitic tumor cell growth: Involvement of NF-κB signaling activation in CD4+ T cells. Toxicology and Applied Pharmacology. 2013;269(3):270–9.
13. Liu Z, Wang S, Zhang J, Wang Y, Wang Y, Zhang L, et al. Gastrodin, a traditional Chinese medicine monomer compound, can be used as adjuvant to enhance the immunogenicity of melanoma vaccines. International Immunopharmacology. 2019;74:105699.
14. Jiang W, Zhang L, Shan W, Wu Z, Wang J, Shen C. Gastrodin promotes osteogenic differentiation by stimulating the Wnt/β-catenin signaling pathway. Molecular and Cellular Probes. 2025:102035.
15. Sharma V, Sharma P, Singh TG. Wnt signalling pathways as mediators of neuroprotective mechanisms: therapeutic implications in stroke. Molecular Biology Reports. 2024;51(1):247.
16. Wu X, Liu Z, Yu XY, Xu S, Luo J. Autophagy and cardiac diseases: Therapeutic potential of natural products. Medicinal Research Reviews. 2021;41(1):314–41.
17. Selfa Aspiroz L, Mennecozzi M, Batlle L, Corneo B, Healy L, Kotter M, et al. Promoting the adoption of best practices and standards to enhance quality and reproducibility of stem cell research. Stem Cell Reports. 2025;20(7).
18. Sobiesiak M, Fatyga N, Brzozowski A, Sikora A, Kupcewicz B, Maj M. Chromanone derivatives: Evaluating selective anticancer activity across human cell lines. Eur J Med Chem. 2025;295:117771.
19. Sung S-E, Seo M-S, Kim Y-I, Kang K-K, Choi J-H, Lee S, et al. Human epidural AD–MSC exosomes improve function recovery after spinal cord injury in rats. Biomedicines. 2022;10(3):678.
20. Bulbul MV, Mermer A, Kolbasi B, Kocabas F, Kalender SM, Kirectepe Aydin KA, et al. mTOR Pathway Inhibition, Anticancer Activity and In Silico Calculations of Novel Hydrazone Derivatives in Two-and Three-Dimensional Cultured Type 1 Endometrial Cancer Cells. Pharmaceuticals. 2024;17(12):1562.
21. Bulbul MV, Karabulut S, Kalender M, Keskin I. Effects of gallic acid on endometrial cancer cells in two- and three-dimensional cell culture models. Asian Pacific Journal of Cancer Prevention: APJCP. 2021;22(6):1745.
22. Xie Z, Zhou H, Ou T, Pei W, Fan X. The Function and Effectiveness of MSCs in Preclinical Models of Diseases. Stem Cell Transplantation: IntechOpen; 2024.
23. Zuo H-J, Wang P-X, Ren X-Q, Shi H-L, Shi J-S, Guo T, et al. Gastrodin regulates PI3K/AKT-Sirt3 signaling pathway and proinflammatory mediators in activated microglia. Molecular Neurobiology. 2024;61(5):2728–44.
24. Li S, Yang Q, Zhou Z, Yang X, Liu Y, Hao K, et al. Gastrodin protects retinal ganglion cells from ischemic injury by activating phosphatidylinositol 3-kinase/protein kinase B/nuclear factor erythroid 2-related factor 2 (PI3K/AKT/Nrf2) signaling pathway. Bioengineered. 2022;13(5):12625–36.
25. Wang J, Wu M. The up-regulation of miR-21 by gastrodin to promote the angiogenesis ability of human umbilical vein endothelial cells by activating the signaling pathway of PI3K/Akt. Bioengineered. 2021;12(1):5402–10.
26. Shih P-C, Tzeng I-S, Chen Y-C, Chen M-L. Gastrodin mitigates ketamine-induced inhibition of F-actin remodeling and cell migration by regulating the rho signaling pathway. Biomedicines. 2025;13(3):649.
27. Liu Y-M, Wu A-D, Chen Y, Ma T-F, Dong B-Z, She Z-G, et al. Gastrodin inhibits prostate cancer proliferation by targeting canonical Wnt/β-catenin signaling pathway. Medical Oncology. 2023;41(1):32.
28. Chavda VP, Nalla LV, Balar P, Bezbaruah R, Apostolopoulos V, Singla RK, et al. Advanced phytochemical-based nanocarrier systems for the treatment of breast cancer. Cancers. 2023;15(4):1023.