

## **$\alpha$ -Linalool from Coriander Root Inhibits the Proliferation and Invasion of Human Gastric Cancer Cells**

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Received: 04 August 2024; Revised: 15 October 2024; Accepted: 19 October 2024

### **ABSTRACT**

This study investigated the biological effects of coriander root extract on gastric cancer cells, specifically focusing on how it affected the proliferation and motility of the BGC-823 cell line. The findings showed that exposure to the extract led to a sharp drop in colony survival and significantly hindered cellular proliferation. In addition, the extract reduced the invasive behavior of the cancer cells, impaired their ability to close scratch wounds, and interfered with their ability to migrate. These results indicated a disruption in the EMT mechanism. Further investigation revealed that coriander root extract suppressed the expression of signaling molecules such as P-GSK-3 $\beta$ , TGF- $\beta$ , and P-SMAD2/3, while it simultaneously upregulated SMAD2/3 and GSK-3 $\beta$ . These shifts in gene activity suggest that the effects of coriander root are mediated through pathways involving  $\beta$ -catenin and the TGF- $\beta$ /SMAD cascade, ultimately affecting proliferation and motility in gastric cancer cells. Furthermore,  $\alpha$ -linalool, one of the primary active components in coriander root, played a central role in curbing both the expansion and infiltration of BGC-823 cells. Overall, the evidence supports the idea that  $\alpha$ -linalool from coriander root targets gastric cancer progression by modulating  $\beta$ -Catenin and TGF- $\beta$ /SMAD signaling pathways, thereby restraining both proliferation and migration.

**Keywords:** Migration, Gastric cancer,  $\alpha$ -Linalool, Coriander root, Proliferation

**How to Cite This Article:** Xie L, Wu Z, Liu Y, Tang J, Lu C, Wang H.  $\alpha$ -Linalool from Coriander Root Inhibits the Proliferation and Invasion of Human Gastric Cancer Cells. Asian J Curr Res Clin Cancer. 2024;4(2):19-31. <https://doi.org/10.51847/74nRbFHbyT>

### **Introduction**

Gastric cancer, a malignant tumor that arises from the epithelial lining of the stomach, remains one of the most prevalent and deadly forms of cancer globally. Epidemiological reports indicate that it ranks fourth in incidence and third in mortality among all cancers, following only lung and liver cancers in lethality [1]. As per the World Health Organization's 2020 report, China accounts for the highest global burden of gastric cancer, with approximately 44.0% of new diagnoses and 48.6% of deaths worldwide [2]. By 2021, the number of newly reported gastric cancer cases reached an estimated 1.05 million globally [3]. In 2022, China alone reported 380,000 new cases [4, 5], positioning the disease among the top three most frequently diagnosed and fatal malignancies in the country. Every year, around 679,000 individuals in China are diagnosed with gastric cancer, with an alarming 498,000 succumbing to the disease. Despite medical advances, the prognosis remains grim with a 5-year survival rate hovering at just 11.6%, reflecting a dire public health challenge and significant socioeconomic strain [6, 7].

Current treatment modalities in China typically involve a combination of surgical intervention, chemotherapy, and radiotherapy. However, the widely used chemotherapeutic agents such as fluorouracil and doxorubicin lack tumor selectivity. While effective in targeting cancerous cells, they also inflict collateral damage on healthy tissues—particularly rapidly dividing cells in bone marrow and hair follicles—leading to serious side effects [8,

9]. In contrast, Chinese herbal medicine, especially formulations derived from both medicinal and edible sources, offers reduced toxicity and is more acceptable to patients. Integrating traditional concepts of diet therapy and holistic health from Chinese medicine with modern pharmacological approaches has emerged as a promising area of focus. These integrated practices are now at the forefront of popular health trends, raising questions about their potential roles in cancer therapy.

In line with global standards, the 2022 guidelines from the National Comprehensive Cancer Network in the United States emphasized a multidisciplinary strategy that includes surgery, perioperative chemotherapy, radiation, immunotherapy, and targeted therapies. Nonetheless, challenges persist, including postoperative metastasis, recurrence, adverse drug reactions, and resistance to treatment. Growing interest has turned toward botanical-based treatments due to their anticancer properties. Many potent therapeutic agents, including artemisinin, schisandrin C, paclitaxel, vincristine, and vinblastine, have been isolated from medicinal plants and are now integral to disease management strategies [10–13].

In the context of traditional Chinese medicine (TCM), recent investigations have validated the efficacy of time-honored herbal formulas, experience-based prescriptions, and bioactive components in managing gastric cancer. For instance, curcumin—a naturally occurring polyphenol—has demonstrated substantial anticancer activity against gastric tumors [14]. TCM's unique contribution to gastric cancer treatment lies in its ability to operate through diverse mechanisms and at multiple physiological levels. Its use has become increasingly prominent, with clinical data supporting its efficacy in alleviating symptoms, halting progression from precancerous states, preventing relapse or spread after surgery, enhancing the outcomes of chemotherapy, and reducing associated toxicity. This underscores the growing anticipation and demand for effective and less harmful TCM-based therapeutic options.

*Coriandrum sativum*, more commonly known as coriander, is a widely utilized culinary herb, valued across numerous global cuisines. This annual herb is characterized by its green, lanceolate foliage, a prominent taproot system, white or pink umbel flowers, and rounded dried seeds. Typically reaching a height of 20–70 cm, coriander is extensively cultivated throughout Africa, Asia, and Europe. Scientific investigations have attributed a diverse range of pharmacological properties to coriander and its bioactive constituents, identifying notable antioxidant, anti-inflammatory, analgesic, neuroprotective, anticonvulsant, and anticancer potential [15–17]. The plant's integration into daily diets alongside its therapeutic relevance positions it as a distinctive type of functional food. The medicinal efficacy of coriander is primarily attributed to its strong antioxidative capabilities, largely driven by compounds such as linalool [18–20].

In a study the anti-proliferative potential of coriander was explored through extracts derived from its roots, leaves, and stems, particularly against the breast cancer cell line MCF-7. Among the different extracts, the ethyl acetate fraction obtained from coriander roots demonstrated the highest concentration of phenolic compounds and exhibited superior antioxidant as well as anti-proliferative activity. Furthermore, this extract suppressed MCF-7 cell migration in a concentration-dependent manner. Additional observations highlighted that coriander leaf extract also suppressed both proliferation and migration in prostate cancer cell lines PC-3 and LNCaP [17].

Another significant contribution by Eid *et al.* involved formulating coriander oil into a nanogel, resulting in a nanoemulsion with a particle size of 165.72 nm and a polymer dispersion index of 0.188. This nanoformulation showed strong cytotoxic effects against multiple human cancer cell lines including MCF-7 (breast cancer), Hep3B (liver cancer), and HeLa (cervical cancer). Similarly, Huang and collaborators studied coriander's influence on HepG2 (a human hepatoma line) and B16F10 (a murine melanoma line), revealing its capacity to significantly inhibit both cell migration and invasion, thereby suggesting a role in improving cancer prognoses.

Devi Khwairakpam *et al.* [21] examined the biological effects of Vietnamese coriander and determined that it exerted anti-proliferative, anti-metastatic, and cell-survival inhibiting properties by inducing G2-phase arrest in the cell cycle. The herb was also found to suppress the AKT-mTOR signaling cascade, leading to the downregulation of multiple oncogenic proteins including cyclin D1, COX2, survivin, VEGF-A, and MMP-9. It was further reported that this variant of coriander interfered with oral cancer progression through a dose-responsive inhibition of the AKT-mTOR pathway [21].

Moreover, corroborating studies have demonstrated coriander's anticancer efficacy across several malignancies, such as colon, breast, and cervical cancers [22, 23]. Despite its broad therapeutic promise, the role of coriander—particularly its root extract—in the context of gastric cancer remains unexplored. The current study therefore aims to bridge this knowledge gap by investigating the effects of coriander root extract on the growth and migratory behaviors of gastric cancer cells. Through molecular biology, immunological assays, and related scientific

techniques, this work seeks to lay a foundational framework for the use of coriander in gastric cancer treatment and prevention.

## Materials and Methods

### *Materials*

Gastric cancer cell line BGC-823 was kindly provided by the Etiology Laboratory at the School of Medicine, Jiangsu University. The DMEM culture medium and fetal bovine serum utilized in this study were sourced from Gibco. Trypsin for cell digestion was obtained from Sigma. Antibodies specific for GAPDH were purchased from Abcam, while the protein marker employed was supplied by Shanghai Biochemical Reagent Co., Ltd. Additionally, antibodies targeting MMP9, MMP2, and PCNA were acquired from Wanke Biological Co., Ltd.

### *Extraction of coriander root*

Fresh coriander roots were cleaned thoroughly and air-dried before weighing. The dried roots were then soaked in an adequate volume of double distilled water for 35 minutes. Subsequently, the sample was boiled in a total of 3 liters of double distilled water using standard procedures employed in traditional Chinese medicine decoction. The extraction process continued until the liquid volume was reduced to 200 ml, at which point heating was halted. The resulting extract was determined to have a concentration of 14.315 mg/ml. The decoction was stored at -20 °C until further experimental application.

### *Determining effective concentration and exposure duration of coriander root extract via cell count assay*

BGC-823, a human gastric cancer cell line, was cultivated under standard conditions of 5% CO<sub>2</sub> at 37 °C. Upon reaching 80–90% confluence, the cells underwent enzymatic digestion, were converted into a single-cell suspension, and counted. A seeding density of  $4 \times 10^4$  cells per well was used to inoculate 12-well plates, followed by overnight incubation at 37 °C in 5% CO<sub>2</sub>. The cells were subsequently treated with coriander root extract at final concentrations of 0.01, 0.02, 0.04, 0.08, and 0.16 mg/ml. Cell numbers were recorded after 24, 48, and 72 hours of treatment, and the relationship between concentration and cell count was visualized by plotting dose-response curves.

### *Assessment of cellular viability using the CCK8 assay following coriander root extract exposure*

In the viability assay, cells were exposed to either DMEM medium alone (control) or DMEM supplemented with varying concentrations of coriander decoction: 0.01, 0.02, 0.04, 0.08, and 0.16 mg/ml. After 48 hours, optical density (OD) values were measured to evaluate the metabolic activity of each group. In an additional experiment, a fixed coriander concentration (0.02 mg/ml) was applied to different cell groups, and OD measurements were collected at multiple intervals (12, 24, 36, 48, and 72 hours) to monitor changes over time.

BGC-823 cells in the logarithmic growth phase were plated in 96-well plates at a density of one thousand cells per well. Each condition was replicated in three independent double-well groups. After cell adhesion occurred overnight, the blank control wells remained untreated. The experimental sets were divided into two parallel protocols. In the first, cells received coriander decoction at the aforementioned concentrations simultaneously, and their OD values were determined after 48 hours. The second protocol maintained a constant coriander decoction concentration of 0.02 mg/ml, and viability was evaluated across multiple time points—specifically at 12, 24, 36, 48, and 72 hours—via OD measurement.

### *Assessment of coriander root extract on cell proliferation via cloning assay*

BGC-823 human gastric cancer cells were plated into 6-well plates, at a density of  $3.0 \times 10^5$  cells per well, during their logarithmic growth phase. After 24 hours, the cells were exposed to either a control condition or treatment with 0.02 mg/ml coriander root extract. After 48 hours of treatment, cells were harvested, digested, and resuspended into a single-cell suspension for counting. From this suspension, 1000 cells were replated in new 6-well plates. The media was refreshed every 3–4 days over 10–12 days. At the end of the incubation, the culture medium was discarded, and cells were washed with PBS before being fixed with paraformaldehyde for 30 minutes. After washing, cells were stained with crystal violet for fifteen minutes at room temperature, followed by PBS washing and drying. Images of the colonies were captured, and the colony formation efficiency was determined.

#### *Coriander root extract's effect on cell migration: transwell assay*

BGC-823 cells in logarithmic growth were plated at a density of  $3.0 \times 10^5$  cells per well in 6-well plates. The next day, the cells were subjected to their respective treatments. After 48 hours, the cells were digested, and a serum-free suspension was prepared.  $1 \times 10^5$  cells were placed in the upper chamber of a transwell insert, and 600  $\mu$ L of serum-containing medium was placed in the lower chamber. The plates were incubated at 37 °C with 5% CO<sub>2</sub> for 24 hours. Following the incubation, cells were fixed with 4% paraformaldehyde for 30 minutes, washed with PBS, and stained with crystal violet for fifteen minutes. Non-migratory cells in the upper chamber were removed with a cotton swab. The cells in the lower chamber were then dried and examined under a microscope. Multiple randomly selected fields (3–4) were photographed for migration analysis.

#### *Extraction of protein from BGC-823 cells*

Logarithmic phase BGC-823 cells were plated at  $3.0 \times 10^5$  cells per well in 6-well plates and treated the following day according to the experimental protocol. After 48 hours, cells were lysed using a protein extraction buffer containing protease inhibitors, and incubated for 30 minutes. Afterward, the lysates were centrifuged at 13,000 rpm for 30 minutes at 4 °C, and the supernatant was mixed with 5x loading buffer (4:1 ratio). The samples were boiled in a water bath at 100 °C for 10 minutes and then stored at -20 °C for future use.

#### *Western blotting analysis of signaling pathway protein expression post-treatment with coriander root extract*

A 10% SDS-PAGE gel was used to separate the protein samples, which were then transferred onto a PVDF membrane at 300 mA for 90 minutes. The membrane was blocked with 5% skimmed milk at room temperature for 2 hours, followed by incubation with the primary antibody at 4 °C overnight. Protein bands were quantified using Image Pro Plus software for further analysis.

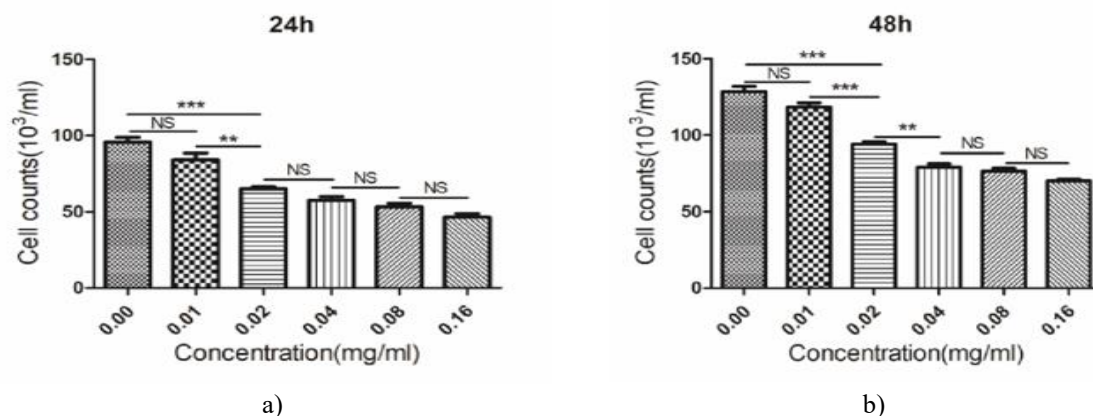
#### *Statistical evaluation*

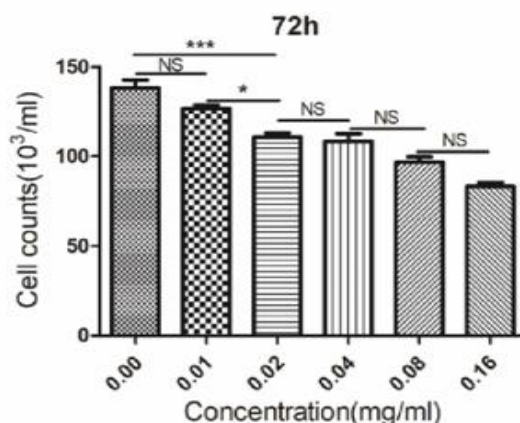
Data were analyzed with GraphPad Prism 5.0 software and presented as mean  $\pm$  standard deviation ( $X \pm SD$ ). Statistical significance between groups was assessed using Student's t-test or one-way ANOVA. The significance levels were: ns (not significant),  $P < 0.05$ ,  $P < 0.01$ , and  $P < 0.001$ .

## Results and Discussion

#### *Optimization of treatment conditions for coriander root extract*

Cell proliferation was evaluated over three different treatment durations: 24, 48, and 72 hours. The cell count data revealed that coriander root extract inhibited the proliferation of BGC-823 gastric cancer cells in a dose-dependent manner when compared to the control group. Statistical analysis showed that the difference in cell count between the 0.02 mg/ml and 0.01 mg/ml drug concentrations was significant ( $P < 0.05$ ) at each time point, with the most pronounced effect observed at 48 hours ( $P < 0.005$ ). Based on these findings, the subsequent experiment (**Figure 1**) was carried out using a 0.02 mg/ml concentration of the extract for a 48-hour treatment period.



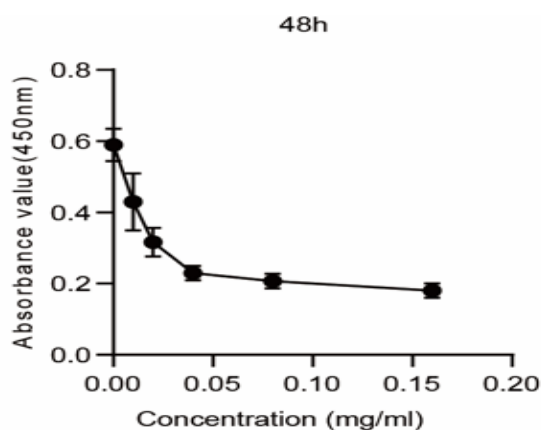


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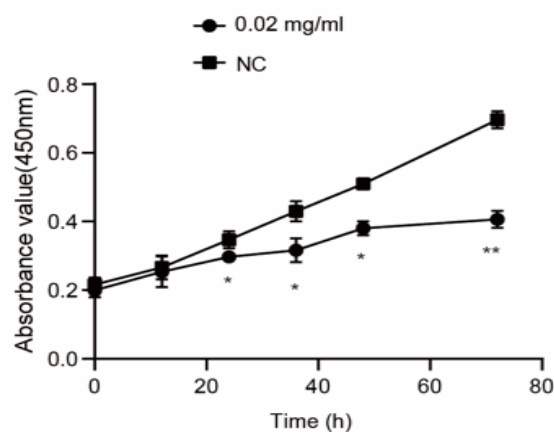
**Figure 1.** Graphical representation of cell count data: (a) impact of various concentrations of coriander extract on the proliferation of BGC-823 gastric cancer cells after 24 hours, (b) effect of different concentrations of coriander extract on the proliferation of BGC-823 cells following 48 hours of treatment, and (c) influence of coriander extract at varying concentrations on the proliferation of BGC-823 gastric cancer cells after 72 hours of exposure; \*  $P < 0.05$ , \*\*  $P < 0.01$ , \*\*\*  $P < 0.001$ .

#### Impact of coriander root extract on gastric cancer cell proliferation

To evaluate the influence of coriander root extract on gastric cancer cell growth, CCK8 assays revealed that coriander root extract effectively inhibited the proliferation of BGC-823 gastric cancer cells in a time- and concentration-dependent manner. Specifically, treatment with a 0.02 mg/ml concentration of the extract for 48 hours resulted in a 50% reduction in cell proliferation compared to the control group. Furthermore, BGC-823 cells displayed moderate vitality, making them an ideal model for further experimental studies and functional assays. Hence, this concentration and treatment duration were chosen as the baseline conditions for subsequent experiments (**Figures 2a and 2b**). Plate cloning assays indicated that after two weeks of culture, BGC-823 cells exposed to 0.02 mg/ml coriander root extract for 48 hours formed significantly fewer clones, with a noticeable reduction in their size (**Figure 2c**) (\*  $P < 0.05$ ).

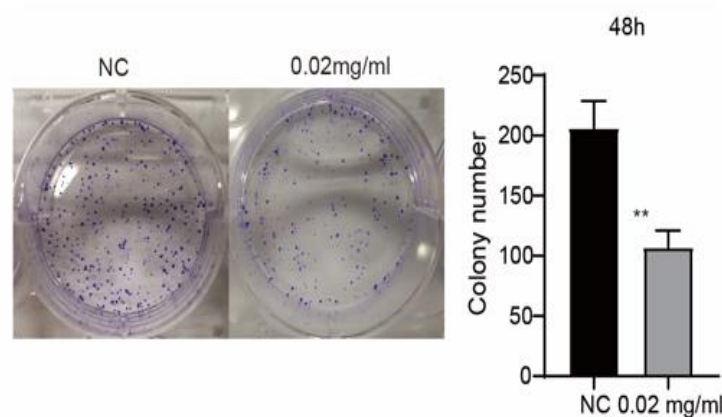


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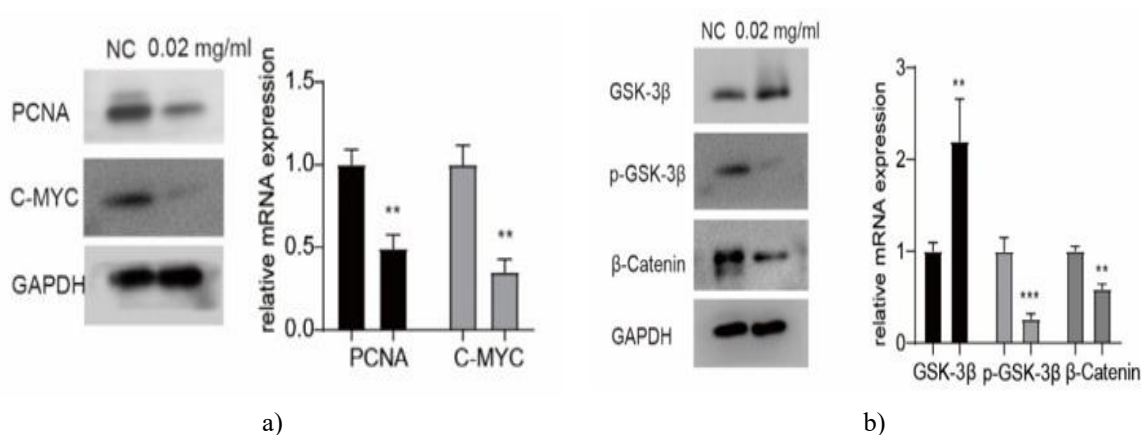
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**Figure 2.** CCK-8 assay analysis of coriander root extract's effect on BGC-823 cell proliferation: (a) the impact of varying concentrations of coriander extract on BGC-823 gastric cancer cell proliferation after 48 hours of treatment, assessed via CCK-8 assay, (b) the effect of a consistent concentration of coriander extract on the proliferation of BGC-823 gastric cancer cells after 48 hours of exposure, measured by CCK-8 assay, and (c) the influence of 0.02 milligrams per milliliter coriander root extract on the clonogenic ability of BGC-823 gastric cancer cells after 48 hours of treatment.

#### *Impact of coriander root extract on the expression of proteins linked to cell proliferation*

To explore the underlying molecular mechanisms responsible for the proliferation-inhibitory effect of coriander root extract on gastric cancer cells, we analyzed the expression levels of proliferation-associated genes. Western blot analysis demonstrated a marked suppression in the expression of PCNA and C-MYC following treatment with coriander root extract at a concentration of 0.02 milligrams per milliliter for 48 hours, in comparison to the untreated group. These findings provide evidence that coriander root extract effectively impedes the proliferation of BGC-823 gastric cancer cells (\*  $P < 0.05$ , \*\*  $P < 0.01$ ) (**Figure 3a**).

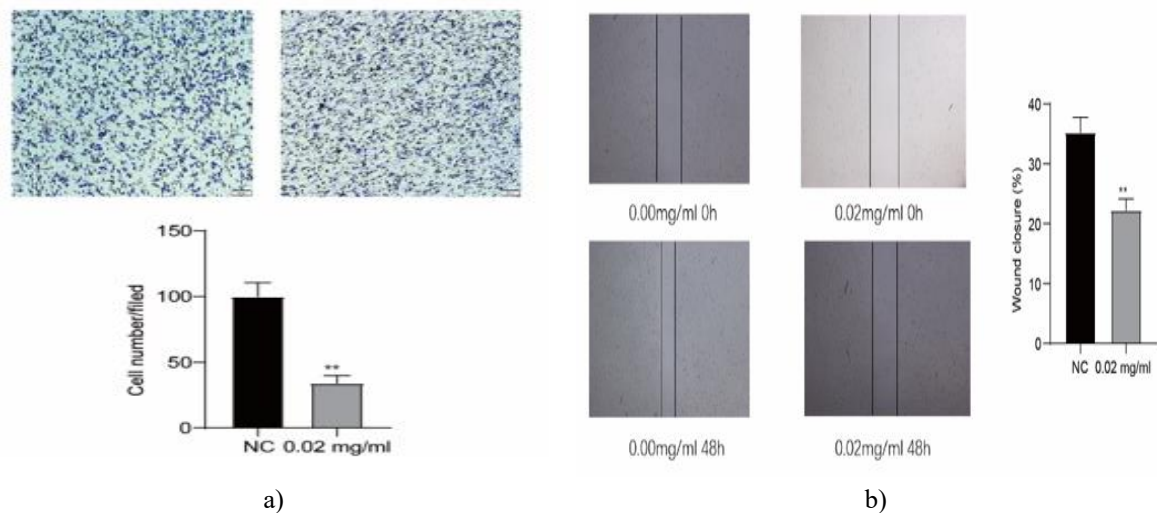
In addition, we examined key components of the  $\beta$ -Catenin signaling pathway, including  $\beta$ -Catenin, GSK-3 $\beta$ , and phosphorylated GSK-3 $\beta$  (P-GSK-3 $\beta$ ). The data revealed downregulation of both  $\beta$ -Catenin and P-GSK-3 $\beta$ , while the expression level of GSK-3 $\beta$  was upregulated when compared with control cells. These results indicate that coriander root extract may exert its anti-proliferative effects through modulation of the  $\beta$ -Catenin signaling axis (\*  $P < 0.05$ , \*\*  $P < 0.01$ ) (**Figure 3b**).



**Figure 3.** Analysis of the impact of coriander root extract on proteins associated with cell proliferation pathways in gastric cancer BGC-823 cells: (a) detection of altered expression levels in proliferation-associated proteins PCNA and C-MYC following treatment, and (b) evaluation of expression variations in proteins linked to the  $\beta$ -Catenin signaling cascade.

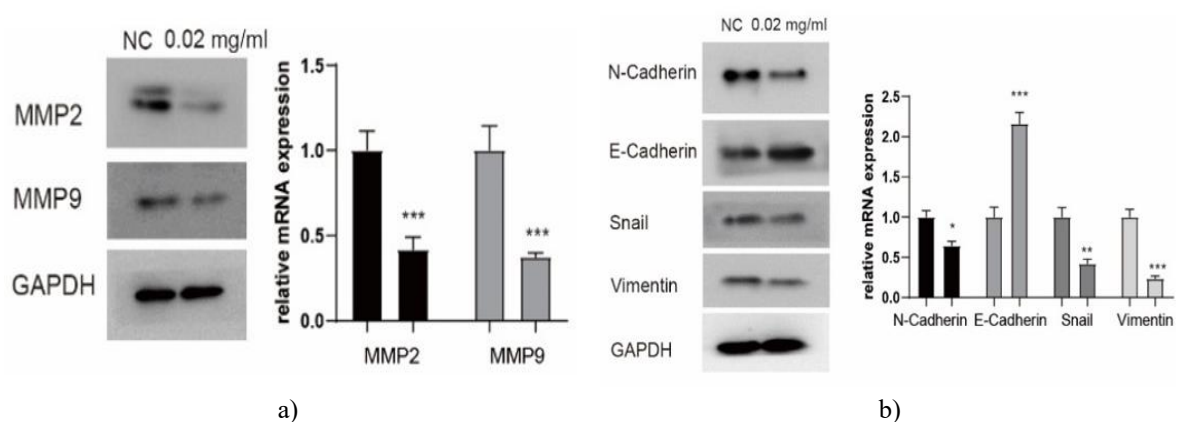
#### *Coriander root extract restricts cell migration and invasion in gastric cancer BGC-823 cells*

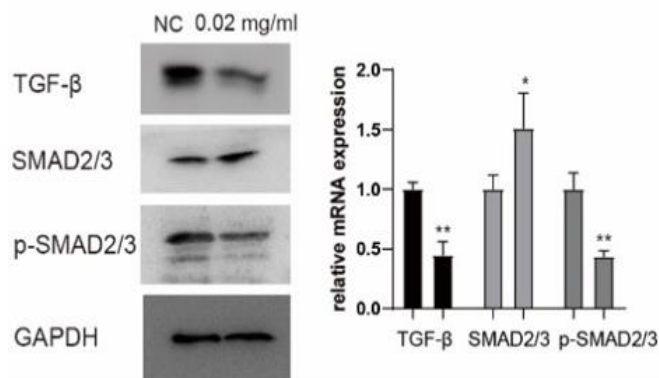
A noticeable decline in the transmembrane passage of BGC-823 cells was observed after exposure to coriander root extract, in stark contrast to the control group. This outcome, visualized in **Figure 4a**, reveals that the extract significantly disrupts the invasive traits of the cells. Similarly, the scratch wound assay produced supporting evidence: the treated cells exhibited a sluggish response in bridging the wound gap, unlike the rapid recovery seen in untreated cells. This diminished scratch repair, illustrated in **Figure 4b**, implies that the coriander root extract substantially weakens the migration potential of gastric cancer BGC-823 cells.



**Figure 4.** Investigation of cell motility following exposure to coriander root extract: (a) a transwell-based approach was utilized to examine alterations in the migration performance of cells after being subjected to coriander root extract at a concentration of 0.02 milligrams per milliliter, and (b) to assess directional movement and repair capacity, a scratch assay was conducted, revealing how 0.02 milligrams per milliliter of coriander root extract influences the cell's ability to close a wound gap.

In addition, several canonical markers linked to cellular invasion were assessed. Western blot analysis revealed a marked downregulation of MMP2 and MMP9 expression levels relative to the control group, alongside an upregulation of the epithelial marker E-cadherin. Conversely, proteins commonly associated with mesenchymal identity—N-cadherin, vimentin, and snail—were significantly diminished. These findings suggest that coriander root extract interferes with the epithelial-mesenchymal transition (EMT) in gastric cancer BGC-823 cells, thereby reducing their invasive capacity (**Figures 5a and 5b**). Moreover, a reduction in TGF- $\beta$  and phosphorylated SMAD2/3 expression was detected, while levels of total SMAD2/3 were notably elevated. Taken together, these observations support the hypothesis that coriander root extract suppresses the invasiveness of BGC-823 cells through modulation of the TGF- $\beta$ /SMAD signaling cascade (\*  $P < 0.05$ , \*\*  $P < 0.01$ , \*\*\*  $P < 0.001$ ) (**Figure 5c**).



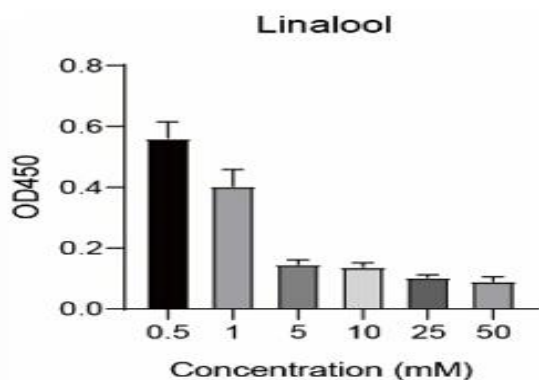


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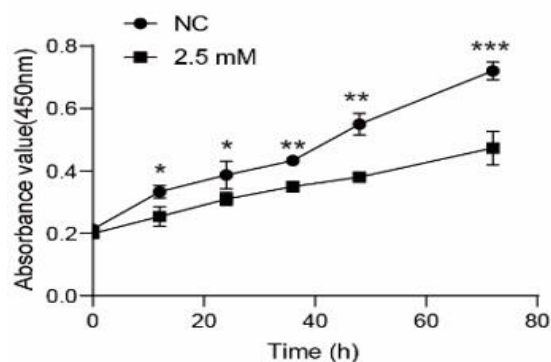
**Figure 5.** Impact of coriander root extract on the invasiveness of gastric cancer cells and the expression of related signaling proteins: (a) alterations in the levels of MMP2 and MMP9 proteins, (b) modifications in the expression of proteins involved in EMT, and (c) variations in the TGF- $\beta$ /SMAD signaling pathway proteins.

#### Impact of $\alpha$ -linalool from coriander root extract on gastric cancer cell proliferation and invasion

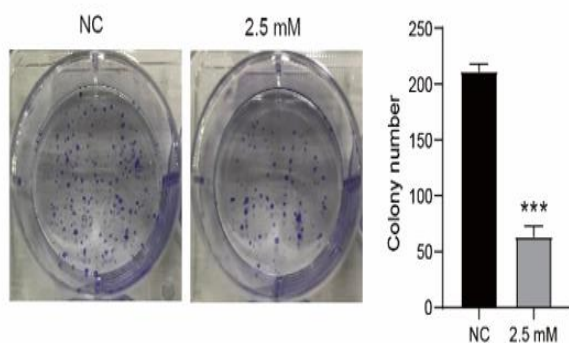
To determine the active component responsible for the effects observed in coriander root extract, we conducted an in-depth experiment. The extract includes several compounds, such as decanal, nonanal, linalool, and vitamin C, with  $\alpha$ -Linalool representing the predominant volatile oil component (approximately 70%). Additionally, other compounds like  $\alpha$ - and  $\beta$ -pinene, dipentene (limonene),  $\alpha$ -,  $\beta$ -, and  $\gamma$ -terpinene, and p-cymene are also present. Given this composition, we specifically focused on  $\alpha$ -Linalool. In vitro cytotoxicity tests demonstrated that treatment with  $\alpha$ -Linalool for 48 hours inhibited cell viability in a concentration-dependent manner (**Figure 6a**). The calculated IC<sub>50</sub> (half-maximal inhibitory concentration) for the BGC-823 gastric cancer cell line was  $3.726 \pm 0.105$  mM. Further analysis revealed that  $\alpha$ -Linalool significantly reduced both the proliferation and migration of BGC-823 cells (**Figures 6b and 6e**). Consequently, these findings indicate that  $\alpha$ -Linalool effectively suppresses the growth of gastric cancer cells.



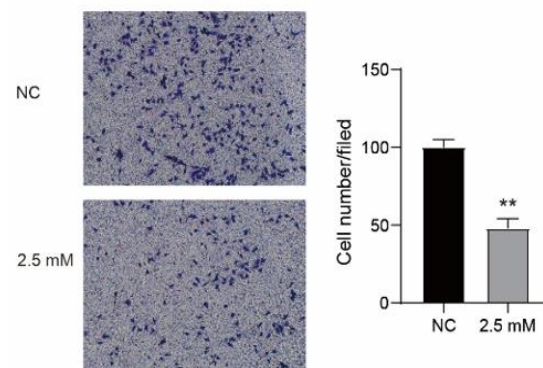
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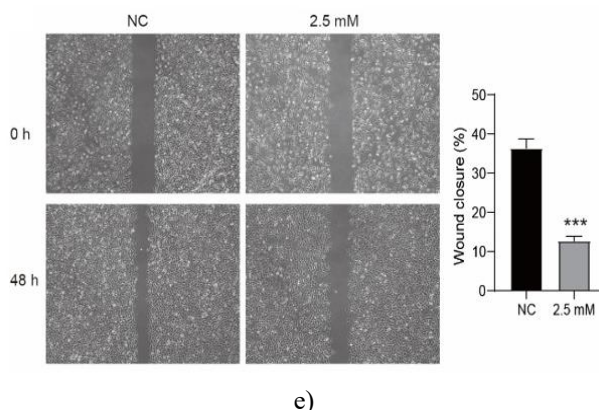


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**Figure 6.** Influence of  $\alpha$ -linalool on the growth and migration of gastric cancer BGC-823 cells: (a) the effect of various concentrations of  $\alpha$ -linalool on the proliferation of BGC-823 cells after 48 hours was measured using the CCK-8 assay, (b) the same assay was applied to evaluate the effect of a 2.5 mM concentration of  $\alpha$ -linalool on the cell proliferation of BGC-823 cells after 48 hours, (c) the ability of BGC-823 cells to form clones after treatment with 2.5 mM  $\alpha$ -linalool for 48 hours was assessed, (d) a transwell migration assay was used to determine how 2.5 mM  $\alpha$ -linalool affects the migratory capacity of gastric cancer BGC-823 cells, and (e) the scratch assay was performed to investigate how 2.5 mM  $\alpha$ -linalool influences the wound healing ability of cells after 48 hours.

Cancer is a condition marked by the uncontrolled expansion and dysfunction of tumor cells, which often arises from metabolic abnormalities within these cells. Tumor cells display distinct characteristics such as accelerated metabolism, rapid division, proliferation, and enhanced migratory ability, contributing to their swift progression once they begin to develop [24, 25]. A critical aspect of cancer progression is the proliferation, invasion, and metastasis of tumor cells, particularly in the later stages of the disease. This progression, including the malignant transformation of human tumors and the metastasis of advanced cancers, has become a primary cause of cancer-related morbidity and mortality [26, 27]. As a result, much of the focus in cancer treatment is directed at inhibiting tumor cell proliferation and invasion.

Current treatment methods for cancer include surgery, chemotherapy, and radiotherapy. However, chemotherapy drugs are often associated with significant systemic toxicity and side effects, which can greatly affect the patient's quality of life [9]. Traditional Chinese medicine offers an alternative, with fewer systemic toxic effects, targeted action, and notable therapeutic efficacy. These advantages have led to the growing application of traditional Chinese medicine in the treatment of malignant tumors. Recently, aromatic compounds in plants have garnered attention due to their roles in antibacterial, antioxidant, anti-tumor, and anti-viral activities, and their ability to enhance drug absorption in the body [28-33]. The root of coriander is known to contain various beneficial aromatic compounds, including furfural, unsaturated fatty acids, and other essential chemicals that are advantageous for human health [34-36].

In this study, we investigated the impact of coriander root extract on the growth and migration of the BGC-823 gastric cancer cell line *in vitro*. The results from CCK-8 and colony formation assays indicated that coriander root extract effectively suppressed the proliferation of BGC-823 cells. Western blot analysis revealed a reduction in the expression of proliferation-related proteins such as PCNA (proliferating cell nuclear antigen) and C-myc.  $\beta$ -catenin, a key component of the cadherin complex, plays a crucial role in cell adhesion and gene expression regulation. In the axin complex, GSK-3 $\beta$  phosphorylates  $\beta$ -catenin, causing its accumulation, which can subsequently activate the Wnt/ $\beta$ -Catenin signaling pathway, potentially leading to tumorigenesis. After treatment with coriander root extract, we observed changes in the expression of key  $\beta$ -catenin signaling proteins, suggesting that the extract may inhibit gastric cancer cell proliferation via this pathway.

Epithelial-mesenchymal transition (EMT) refers to the morphological transformation of epithelial cells into mesenchymal cells, granting them migratory capabilities. EMT plays an essential role in normal developmental processes, wound healing, and, notably, the development of malignant tumors [37-39]. It enhances cellular invasiveness, promotes stem cell-like features, and inhibits apoptosis, all of which can contribute to tumor progression. Our Western blot analysis showed that coriander root extract significantly inhibited EMT in BGC-823 cells. Further studies have displayed that tumor cells secrete matrix metalloproteinases (MMPs), which

degrade the cell basement membrane and facilitate tumor invasion. Both Transwell migration assays and scratch tests confirmed that coriander root extract inhibited the invasion of gastric cancer cells. Western blot results also revealed reduced expression levels of MMP2 and MMP9. Additionally, the TGF- $\beta$ /SMAD signaling pathway was affected by the extract, with decreased levels of P-SMAD2/3 and increased levels of SMAD2/3, further supporting the hypothesis that coriander root extract regulates gastric cancer cell invasiveness through this pathway.

Linalool, a naturally occurring terpene alcohol found in various fruits, herbs, and spices, has demonstrated antibacterial, anti-inflammatory, and antioxidant properties. Furthermore, it has been identified as having potential anti-cancer effects against various cancers, including colon, prostate, leukemia, and cervical cancer [40-42]. Linalool's anticancer mechanisms may involve apoptosis induction, oxidative stress, cell cycle arrest, and immune modulation [43]. In prostate cancer cells (DU145 and PC-3), linalool has been shown to induce cell cycle arrest and activate apoptosis through a death receptor-dependent pathway. It also inhibits the phosphorylation of ERK1, JNK, and p38 proteins from the mitogen-activated protein kinase family and prevents the activation of the NF- $\kappa$ B/p65 complex, protecting cells from oxidative damage. Furthermore, linalool induces the secretion of several cytokines, including interferon  $\gamma$ , IL-13, IL-2, IL-21, IL-21R, IL-4, IL-6sR, and TNF- $\alpha$ . In leukemia cells, linalool upregulates P53 and cyclin-dependent kinase inhibitors, while also activating caspase-3 and caspase-9 to promote apoptosis in glioma cells [44-49].

## Conclusion

This research aimed to examine the anti-proliferative effects of linalool on gastric cancer cells and to explore its mechanisms of action. The effectiveness of this compound was assessed using in vitro cell line models [44-49]. Based on the findings,  $\alpha$ -linalool, derived from coriander root extract, appears to inhibit the growth and migration of BGC-823 gastric cancer cells through modulation of the  $\beta$ -catenin and TGF- $\beta$ /SMAD pathways. However, further investigation is necessary to comprehensively understand its specific molecular mechanisms in gastric cancer. Coriander root holds potential as a novel candidate for clinical strategies targeting the prevention and management of gastric cancer.

**Acknowledgments:** We extend our sincere gratitude to the editors and anonymous reviewers for their valuable contributions to the review process of this manuscript.

**Conflict of Interest:** None

**Financial Support:** This research was supported by the Zhishan Scholars Program at Southeast University (2242021R41070).

**Ethics Statement:** The experimental procedures were carried out following the ethical guidelines approved by the human welfare committees of Beijing Hospital of Integrated Traditional Chinese and Western Medicine.

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