

Effects of curcumin on the role of MMP-2 in endometrial cancer cell proliferation and invasion

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Abstract. – OBJECTIVE: This study aims to investigate the effect of curcumin concentrations on the proliferation and invasion of endometrial cancer cells.

MATERIALS AND METHODS: Endometrial cancer cells were cultured with 0, 15, and 30 $\mu\text{mol/l}$ curcumin, and were divided into control group, low concentration group, and high concentration group. The treatment included the silencing and overexpression of MMP-2. The expression of MMP-2 and E-cadherin were detected by Western blot and the expression level changes were recorded after MMP-2 was silenced and overexpressed. Pearson's analysis was used to determine the relationship of curcumin concentration between MMP-2 mRNA. CCK-8 was used to detect the optical density of cancer cells in three groups. Transwell invasion assay was performed to analyze the invasion inhibition rate in the three groups.

RESULTS: Western blot and qPCR results: MMP-2 expression levels were lower and E-cadherin was higher in high concentration group than that in the low concentration group ($p < 0.01$). MMP-2 protein and mRNA decreased after ShRNA and increased after overexpression ($p < 0.01$). Pearson analysis revealed that the curcumin concentration was negatively correlated with the MMP-2 mRNA ($r = -0.497$, $p = 0.036$). Cell optical density was lower with curcumin and the lowest was in high concentration group ($p < 0.01$). After MMP-2 silencing, optical cell density decreased and this value increased after overexpression ($p = 0.000$). Cell invasion results: Curcumin improves the rate of cell invasion ($p < 0.01$). After silencing of MMP-2, cell invasion inhibition rate increased, while the invasion inhibition rate decreased after overexpression ($p < 0.01$).

CONCLUSIONS: Curcumin can downregulate MMP-2, inhibit the proliferation and invasion of cancer cells.

Key Words:

Curcumin, Endometrial cancer, Matrix metalloproteinase-2.

Introduction

Endometrial cancer is a group of epithelial malignancies that occur in the endometrium, which occurs in premenopausal and postmenopausal women^{1,2}. In recent years, with the change of human lifestyle, the incidence of endometrial cancer has increased year by year, becoming one of the common gynecological malignancies that lead to female death. At present, the main clinical treatment for endometrial cancer is surgery and chemotherapy. However, common complications after surgery and the unknown mechanism of malignant cancer cell proliferation, invasion, and muscle infiltration often makes treatment less desirable³, resulting in higher patient mortality. To further improve the treatment program and patient prognosis, the basic research direction of clinical search at present is to explore the pathogenesis of cancer, cancer cell proliferation and invasion, and other influencing factors.

The research on cancer cell proliferation and invasion factors has attracted much attention in recent years. Among these, matrix metalloproteinase (MMP) has become a focus of research due to its ability to inhibit tumor cell invasion and metastasis. A large number of studies^{4,5} have shown that MMP can degrade the extracellular matrix (ECM) in a large number of protein components, and play a key role in the tumor development process. Related literature^{6,7} reported that the NF-Kb/MAPK signaling pathway can downregulate MMPs that inhibit cancer cell proliferation and metastasis, inducing apoptosis in cancer cells. This suggests that MMP plays an important role in the proliferation of endometrial cancer cells.

Curcumin is a chemical component extracted from the rhizomes of a plant. In addition to its use in food processing, modern medical research has confirmed that curcumin has hypolipide-

mic, antitumor, and anti-oxidation effects⁸. Recent studies have also found that curcumin has strong tumor inhibitory activities, which further confirms its antitumor effect. At present, curcumin and digestive system tumors, breast cancer and other tumor cell proliferation, invasion and metastasis have been extensively investigated⁹, as well as its relationship with the development of endometrial cancer. However, the study on the mechanisms of cancer cell proliferation and invasion remains non-exhaustive. In addition, MMP is an important factor that affects the invasion and metastasis of cancer cells, and this is most likely associated with the effect of curcumin on the proliferation of endometrial cancer cells. Therefore, this work aimed to investigate the molecular changes of endometrial carcinoma cells under different concentrations of curcumin, in order to further explore the molecular mechanism of curcumin on the proliferation of cancer cells, to find a potential object for the treatment of endometrial cancer.

Materials and Methods

Experimental Materials and Instruments

Ishikawa human endometrial cancer cells were provided by the Cell Bank of the Chinese Academy of Sciences. Curcumin standard (20Mg) was purchased from Shanghai Yuanye Bio-Technology Co., Ltd.. Dulbecco's Modified Eagle Medium (DMEM)-F12, fetal bovine serum and phosphate-buffered saline (PBS) balance solution were purchased from Hyclone (GE Healthcare Life Sciences, HyClone Laboratories, South Logan, UT, USA). The 96-well chamber and trypsin were all purchased from Beyotime Biotechnology. Rabbit anti-human E-cadherin monoclonal antibody, anti-human matrix metalloproteinase-2 (MMP-2) monoclonal antibody, and horseradish peroxidase-labeled goat anti-rabbit secondary antibody were purchased from Shanghai ExCell Bio Co. Ltd. The primers and the reverse transcription kit were purchased from Hanbio Biotechnology Co. Ltd. Instruments include: Cell Counting Kit-8 (CCK-8; Dojindo, Japan); StepOnePlus Real-Time PCR System (Applied Biosystems, Foster City, CA, USA); Western Blotting Analysis System (GE Healthcare Life Sciences, HyClone Laboratories, South Logan, UT, USA); WD-9413A gel imaging analyzer; MD spectraMax M5 full-wavelength microplate reader (Molecular Devices, Jan Jose, CA, USA); inverted microscope; centrifuge.

Cell Culture

Ishikawa cells were cultured in DMEM-F12 medium containing 10% fetal bovine serum at 37°C with 5% CO₂ until adherent growth. Then, the status of these cells was observed until cells reached 80% confluence. The cells were digested with 0.25% trypsin and passaged, and their logarithmic growth phase was tested.

Cell Treatment and Groupings

The curcumin solution was prepared. After the pre-screening test, the experimental design concentration gradients used were 0 μmol/l, 15 μmol/l, and 30 μmol/l. Accordingly, cells were divided into three groups: (1) experimental control group, experimental cells were treated with 0 μmol/l of curcumin; (2) low concentration group, experimental cells were treated with 15 μmol/L of curcumin; (3) high concentration group, experimental cells were treated with 30 μmol/l of curcumin.

Subsequent Treatment of Cells

The subsequent treatment of cells includes blank adenovirus vector infection, MMP-2 silencing, and MMP-2 overexpression. All adenoviral vectors were constructed and carried out by Sinogenomax (Beijing, China). The ShRNA interference MMP-2 adenovirus sequence was designed as 5'-CCGGGCTGAAGGACACACTAAA-GAACTCGAGTTCTTTAGTGTGTCCTTCA-GCTTTTTG-3'. After 24 hours of infection, dose screening of stably transfected cells was conducted, cells were stored at 37°C, and 5% of cells were placed in an incubator for further culture.

Detection of Endometrial Cancer Cell Proliferation by CCK-8

The above three groups of cells were placed in 96-well plates, and approximately 100 μl of cell suspension per well was incubated at 37°C with 5% CO₂ for 24 hours. After adding 10 μl of the CCK-8 solution to each hole for a period of time, the subsequent treatment of cells was performed. The optical density (OD) of different concentrations of curcumin was determined using a full-wavelength microplate reader at 450 nm. The concentration was plotted as the abscissa, and the OD values of each group are plotted as the ordinate. Then, changes in the 6d proliferation situation of the three groups of cells and the proliferation situation after subsequent treatment were observed. The proliferation of cells was calculated by averaging the five holes. The experiment was repeated in triplicate.

Transwell Invasion Assay

Cell invasion: matrigel glue diluted at 7:1 was used to cover the upper chamber of the transwell. Then, 100 μ l of 0.25% trypsin-digested cell suspension was added to the chamber, and 600 μ l of medium containing 100 ml fetal bovine serum was added to the lower chamber. Cells were cultured with 5% CO₂ at 37°C for 24 hours and were removed from the transwell chamber. Then, the culture medium in the hole was discarded, washed two times with PBS, fixed with methanol for 30 minutes, and air dried. Next, cells were dyed with 0.1% crystal violet for 20 minutes, non-migratory cells from the upper layer were gently wiped, cells were washed with PBS, cells were observed and counted in five fields at 400 \times magnification, and the average value was taken. The experiment was repeated in triplicate. Cell invasion inhibition rate was calculated as follows: cell invasion inhibition rate (%) = (1 – the number of cells in the invasive group / the number of cells in the control group) \times 100%.

Western Blot

Cells were trypsin-digested, washed with PBS two times, lysed with radioimmunoprecipitation assay (RIPA) lysis buffer, oscillation centrifugation, and the protein supernatant was collected. In the different concentrations of cells treated under each group, 30 μ g of protein sample were used for sodium dodecyl sulphate-polyacrylamide gel electrophoresis (SDS-PAGE) gel electrophoresis at a constant voltage of 100 V for approximately 120 minutes and a constant current transfer of 300 mA for 60 minutes onto the polyvinylidene difluoride (PVDF) film, and blocked by 5% skim milk for two hours. Then these were added with primary antibody diluent as E-cadherin rabbit anti-human monoclonal antibody and rabbit anti-human MMP-2 monoclonal antibody and incubated overnight at 4°C. After washing the film with Tris-buffered saline (TBS), cells were incubated with horseradish peroxidase-labeled goat anti-rabbit IgG secondary antibody at room temperature for one hour and washed three times with TBS.

Real-Time Quantitative PCR

After 24 hours of cell transfection, TRIzol solution was added, blowing mixed and cells were lysed. Then, 200 μ l of chloroform was added to fully oscillate, cells were centrifuged for 15 minutes, and the supernatant was collected. Next, an equal volume of isopropanol was added to the supernatant. After centrifugation for 10 minutes, the RNA precipitate was collected, washed with 75% ethanol, dried on a clean bench, and then, an amount of Diethyl pyrocarbonate (DEPC) was added to dissolve the precipitate. Reverse transcription was used to synthesize cDNA, and next amplified for 40 cycles. DNA fluorescent dye SYBR Green was used, and β -actin was used as the internal reference gene. For the relative quantitative representation of the experimental results, the target gene was calculated using 2^{- $\Delta\Delta$ CT}. The experiment was repeated in triplicate. The q-PCR primers designed for the experiment are shown in Table I.

Statistical Analysis

SPSS 19.0 statistical software (IBM Corp., IBM SPSS Statistics for Windows, Armonk, NY, USA) was used for statistical analysis. The expression level of MMP-2 and E-cadherin in the three groups of cells was compared by single factor analysis of variance and multiple comparisons between the groups was performed; the post-hoc test was S-N-K method. Then, the effect of curcumin on the expression of MMP-2 and E-cadherin was analyzed. Pearson's correlation analysis revealed a relationship between curcumin concentration and MMP-2 content. To study the effect of curcumin concentration and MMP-2 on the proliferation of cancer cells, repeated measures analysis of variance was performed. Results revealed that there were differences in cell proliferation activity in the three groups when treated with 0 μ mol/l, 15 μ mol/l, and 30 μ mol/l of curcumin for six days. The proliferation activity of these three groups of cancer cells was compared again after MMP-2 silencing and MMP-2 overexpression. Changes in the invasion rate of cancer cells under different concentrations of curcumin and sub-

Table I. Primer sequence for real-time fluorescent quantitative PCR.

Prime	Sequence (5'-3')	
MMP-2	F) TACGATGGAGGCGCTAATGG	R) CAGGTATTGCACTGCCAACTC
E-cadherin	F) ACAGCACGTACACAGCCCTA	R) CAGAAGTGTCCCTGTTCCAG
β -actin	F) TTGCGTTACACCCTTTCTTG	R) ACTGCTGTACCTTCACCG

sequent cell treatments were analyzed by *t*-test. $p < 0.05$ was considered statistically significant.

Results

The Results of Western Blot in Each Group

The Western blotting results are shown in Figure 1. Single factor analysis of variance showed that there were significant differences among the three groups in the protein content of MMP-2 and E-cadherin ($p < 0.05$). After curcumin treatment, compared with that in the control group, MMP-2 protein expression in cells significantly decreased, while E-cadherin protein expression in cells increased significantly by S-N-K method. Real-time fluorescence quantitative PCR results revealed that the mRNA expression of MMP-2 was lower in the low concentration group and high concentration group, compared with that in the control group by S-N-K method, respectively, while the mRNA expression of E-cadherin increased, and the differences were statistically significant ($p < 0.01$). In the high concentration and low concentration groups, results of S-N-K method revealed that the mRNA expression of MMP-2 in the high concentration group was lower, while the mRNA expression of E-cadherin higher ($p < 0.01$; Figures 2).

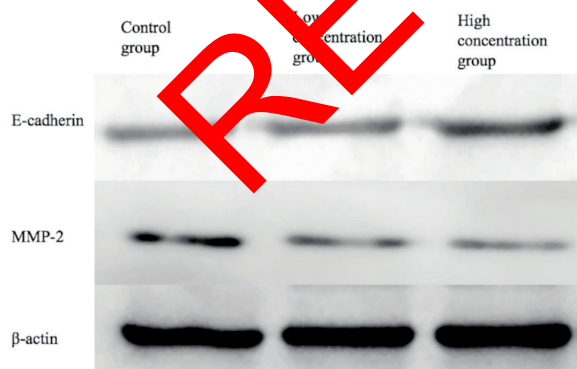


Figure 1. The expression of MMP-2 and E-cadherin in cancer cells in the control group, high concentration group, and low concentration group. The expression of MMP-2 protein in the low concentration group and high concentration group was lower than that in the control group and the high concentration group was lowest; the protein expression of E-cadherin increased; and the difference was statistically significant ($p < 0.01$).

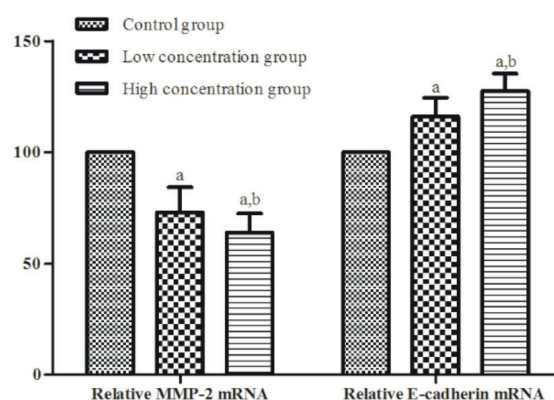


Figure 2. The expression of MMP-2 and E-cadherin mRNA in each group. The expression of MMP-2 mRNA in the low concentration group was lower than that in the control group, while the E-cadherin mRNA in low concentration group was higher and the difference was statistically significant ($^a p < 0.001$). The expression of MMP-2 mRNA in the high concentration group was lower than that in the low concentration group while the E-cadherin mRNA was higher and the difference was statistically significant ($^b p < 0.001$).

Endometrial Cancer Cells With Silenced and Overexpressed MMP-2 Genes

In cells treated with 15 $\mu\text{mol/l}$ of curcumin, MMP-2 protein and mRNA significantly decreased.

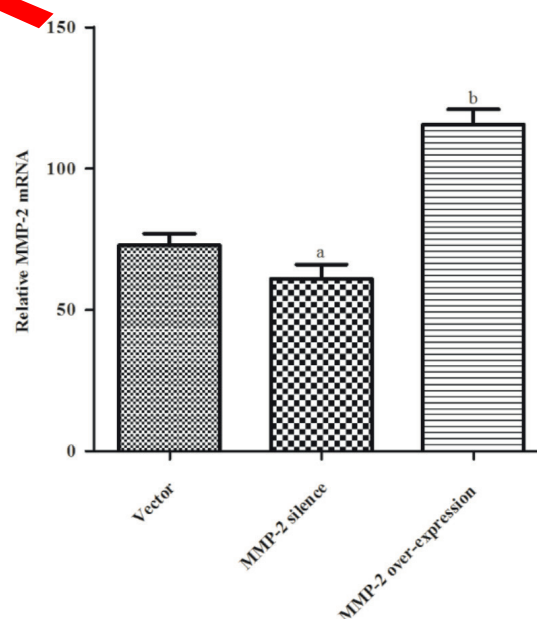


Figure 3. The differences of MMP-2 expression in endometrial cancer cells after the silencing and overexpression of MMP-2. Compared with the vector, the expression of MMP-2 mRNA significantly decreased in cancer cells after MMP-2 silencing and the difference was statistically significant ($^a p < 0.001$). Compared with the vector, the expression of MMP-2 mRNA significantly increased in cancer cells after overexpression and the difference was statistically significant ($^b p < 0.001$).

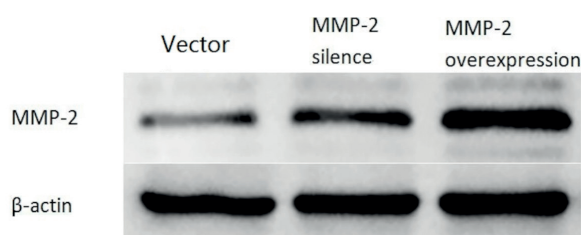


Figure 4. The results of Western blot in endometrial cancer cells after the silencing and overexpression of MMP-2. Compared with the vector, the expression of MMP-2 protein decreased in cancer cells after MMP-2 silencing and it increased after MMP-2 overexpression.

sed in cancer cells after MMP-2 silencing, compared with the vector, and the difference was statistically significant ($p < 0.01$). After overexpression treatment, MMP-2 protein and mRNA expression significantly increased, and the difference was statistically significant ($p < 0.01$) (Figures 3 and 4).

Correlation Analysis

The relationship between curcumin concentration and MMP-2 mRNA expression was further analyzed. Pearson's correlation analysis revealed that the increase in curcumin concentration was negatively correlated with the increase in MMP-2 mRNA expression ($r = -0.497$, $p = 0.036$) (Figure 5).

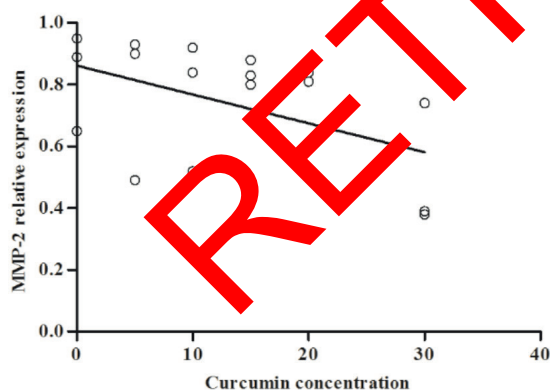


Figure 5. Correlation analysis between curcumin concentration and MMP-2 mRNA. Curcumin concentration was negatively correlated with the expression of MMP-2 mRNA and the difference was statistically significant.

Figure 6. Effect of curcumin concentration on the optical density of cancer cells. Compared with that in the control group, the cancer cell optical density in the low concentration group and high concentration group decreased, and the difference was statistically significant ($p < 0.005$). Compared with that in the low concentration group, the cancer cell optical density in the high concentration group decreased, and the difference was statistically significant ($p < 0.005$).

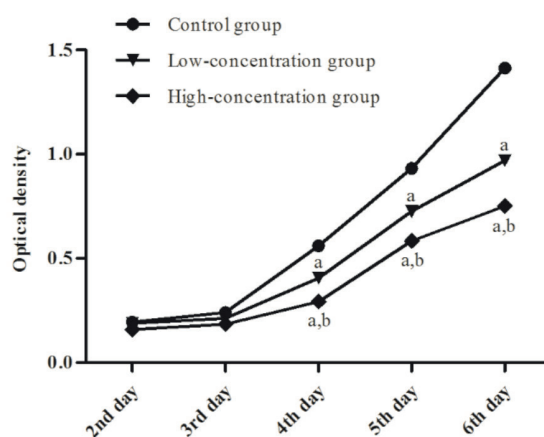


Figure 6. Effect of curcumin concentration on the optical density of cancer cells. Compared with that in the control group, the cancer cell optical density in the low concentration group and high concentration group decreased, and the difference was statistically significant ($p < 0.005$). Compared with that in the low concentration group, the cancer cell optical density in the high concentration group decreased, and the difference was statistically significant ($p < 0.005$).

Cell Proliferation Activity Results

CCK-8 test results revealed that, compared with that in the control group, at curcumin concentrations of 0 $\mu\text{mol/l}$, 15 $\mu\text{mol/l}$, and 30 $\mu\text{mol/l}$, the endometrial cancer cell optical density decreased. Furthermore, repeated measures analysis of variance revealed that the difference between these two groups was statistically significant ($p < 0.05$). Moreover, compared with that in the high concentration and low concentration groups, optical density decreased more significantly, and the difference was statistically significant ($F = 4.829$, $p = 0.000$). Among the different time points, there were differences in optical density among the three groups of cells. After cell incubation on day 4, 5, and 6, optical density significantly decreased in the high concentration and low concentration groups, compared with that in the control group ($p < 0.01$). On the second day after culture, there was no significant difference in optical density among these three groups ($p > 0.05$). Furthermore, optical density was slightly lower in the high concentration group, compared with that in the low concentration group, and the difference was statistically significant ($p < 0.01$) (Figure 6).

Optical Density in Cells After MMP-2 Silencing and Overexpression

After shRNA treatment in the low concentration group, compared with the vector, the

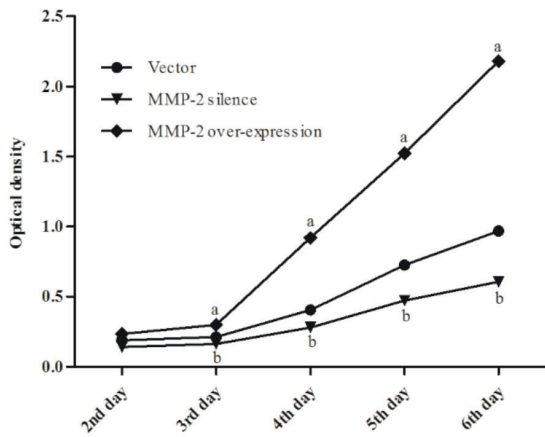


Figure 7. Effect of the downregulation and upregulation of MMP-2 genes on the optical density of cancer cells. Compared with the vector, the cancer cell optical density increased when MMP-2 was overexpressed in cells, and the difference was statistically significant ($^a p < 0.005$); this value decreased when MMP-2 was silenced ($^b p < 0.005$).

absorbance value of cancer cells significantly decreased ($F=7.305$, $p=0.000$), while this value increased when MMP-2 was overexpressed ($F=6.411$, $p=0.000$). Among the different culture time periods, the absorbance value decreased when MMP-2 was silenced in cells, and the difference was statistically significant ($p < 0.05$); while optical density increased when MMP-2 was overexpressed in cells, and the difference was statistically significant ($p < 0.05$) (Figure 7).

Cancer Cell Inhibition Rate

The single factor analysis of variance showed that the three groups of cancer cell invasion inhibition rate was not the same, and the differences were statistically significant ($p < 0.01$). From the comparison with two groups by S-N-K method, the inhibition rate was higher in the high concentration group than in the low concentration group, and this rate was higher than that in the control group, and the difference was statistically significant ($p < 0.01$). In the low concentration group, ShRNA silencing of MMP-2 and overexpression treatment were carried out on cells. It was found that after MMP-2 silencing, cancer cell invasion inhibition rate increased by 22%, while after MMP-2 overexpression, cancer cell invasion inhibition rate decreased by 15%; and the differences were statistically significant ($p < 0.01$) (Figures 8 and 9).

Discussion

At present, there are nearly 200,000 new endometrial cancer cases in China every year, and its high morbidity and mortality rate has brought great burden to society. Endometrial cancer is common in middle-aged women, and postmenopausal irregular vaginal bleeding is its significant early clinical manifestation^{10,11}. As a common gynecological malignancy, endometrial cancer treatment and prognosis has been a point of concern in clinic. At present, surgery, radiotherapy, chemotherapy, and other methods have been mainly used to treat endometrial cancer in clinic. However, the prognosis is not ideal. The main reasons are that cancer cells cannot be controlled, its value-added and invasion mechanism remains unknown. The present study revealed that the MMPs family, transforming growth factor, vascular endothelial growth factor, and cell adhesion factor are closely correlated with the proliferation, invasion, and metastasis of cancer cells. Among these, MMPs, as a result of classification, have a wide effect, play an important role in the invasion and

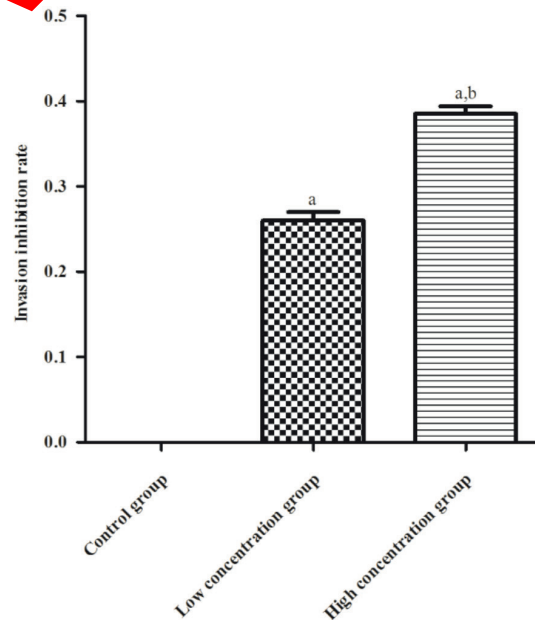


Figure 8. Effect of curcumin concentration on the invasive inhibitory rate of cancer cells. Compared with that in the control group, the inhibition rate in the low concentration group and high concentration group was higher, and the difference was statistically significant ($^a p < 0.005$). Compared with that in the low concentration group, the inhibition rate in the high concentration group was higher, and the difference was statistically significant ($^b p < 0.005$).

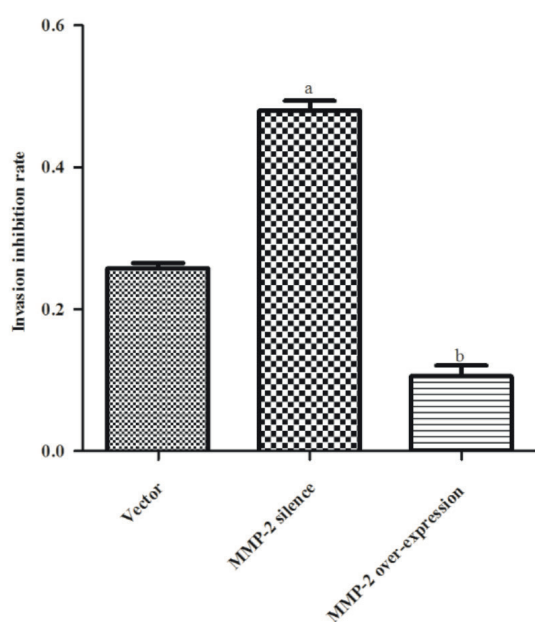


Figure 9. Effect of the downregulation and upregulation of MMP-2 genes on the invasive inhibitory rate of cancer cells. Compared with the vector, the inhibition rate increased after MMP-2 silencing, and the difference was statistically significant (^a $p < 0.005$); this value decreased after MMP-2 overexpression (^b $p < 0.005$).

metastasis of a variety of tumor cells and have become a focus in clinical research. Scholars^{12,13} have revealed that the downregulation of MMP-2 is closely related to the inhibition of the proliferation of endometrial cancer cells.

Curcumin is a natural pigment that has been commonly used in traditional Chinese medicine. Over the past decades, it has been mainly used for food coloring and as an acid-base indicator¹⁴. However, in recent years, its anti-bacterial, hypolipidemic, antioxidant effect has gradually been excavated. Recently authors¹⁵⁻¹⁷ have also found that curcumin has an anti-tumor effect, and its relationship with a variety of tumors has been reported. However, the effect of curcumin in endometrial cancer has been reported rarely. Therefore, regarding the role of MMP-2 in the proliferation and invasion of endometrial carcinoma cells, the investigator further studied the effect of curcumin on endometrial cancer cells, the changes in cancer cell proliferation and invasion capacity, and explored the relationship of this change with the MMP-2 gene.

In general, the gene transcription product is mRNA, and the translation product is a protein or polypeptide. Through detecting mRNA and its

corresponding protein phase, the level of expression of the target gene can be estimated to a certain extent. E-cadherin is one of the important members of the cadherin family. It maintains a close intercellular connection, plays an important role in preventing invasion and metastasis cell activities, and is closely correlated to the proliferation and metastasis of cancer cells. In the laboratory, E-cadherin expression product content is often detected to indirectly reflect the metastasis of cancer cells. In the present work, MMP-2 and E-cadherin protein relative content were detected in cells at different concentrations by Western blotting, while MMP-2 and E-cadherin mRNA content were determined by Q-PCR. Test results revealed that after curcumin treatment, MMP-2 protein and mRNA in cancer cells significantly decreased; and this decrease was more evident in the high concentration group than in the low concentration group. This suggests that curcumin may affect the expression of the MMP-2 gene. There may be a relationship between the change in concentration and the change in MMP-2 content, which changes in E-cadherin protein and mRNA were opposite to that of MMP-2. This suggests that curcumin may affect the selective aggregation and metastasis of cancer cells.

The relationship between curcumin concentration and MMP-2 content was further studied. Pearson's correlation analysis revealed that the increase in curcumin concentration was negatively correlated with the increase of MMP-2 expression. This again suggests a possible relationship between curcumin and MMP-2. Furthermore, some of the effects of curcumin may be mediated by the regulation of MMP-2. Complex Western blot detection results, Real-time fluorescence quantitative PCR results, and correlation analysis results revealed that curcumin has a certain impact on cancer cell growth and metastasis, and this effect is most likely mediated by the regulation of MMP-2 gene expression.

One of the manifestations of malignant tumors is the malignant proliferation of cancer cells. It occurs fast and can be carried out infinitely. The regular disruption of normal cell structure is its typical characteristic. At present, cell proliferation often reflects the size and degree of growth of cell metabolism. Therefore, the proliferation of cancer cells is often measured in clinic, to help to determine the tumor growth status for timely treatment and the inhibition of further tumor growth. In the present study, the CCK-8 test was used to detect the optical density of cancer cells after dif-

ferent treatments, in order to reflect factors that might affect the proliferation of cancer cells and its possible mechanism. Results revealed that curcumin can reduce the optical density of endometrial cancer cells. This suggests that curcumin, in the proliferation of cancer cells, may have an inhibiting effect on tumor growth. Further research on the relationship between the concentration of curcumin and the proliferation of cancer cells revealed that the optical density of cancer cells treated at high concentrations was significantly lower than that in low concentration-treated cancer cells. This suggests that the inhibition effect of curcumin on the proliferation of endometrial cancer cells may be correlated with the concentration. After the shRNA silencing of MMP-2 in cancer cells in the low concentration group, this was compared with the blank vector transfected cancer cells in the low concentration group. It was found that, when the MMP-2 gene was downregulated, cancer cell density significantly decreased; and while the MMP-2 gene was upregulated, cells optical density significantly increased. This means that MMP-2 may affect the proliferation of cancer cells. The present analysis of MMP-2 and tumors were consistent with the results of a large number of reports. Based on the above results, it can be observed that curcumin and MMP-2 downregulation have the potential to inhibit the proliferation of cancer cells, and MMP-2 may be involved in the proliferation process of curcumin-controlled cancer cells.

The invasive inhibition rate of the three groups of cancer cells was further studied by transwell invasion assay. Results revealed that, compared with that in the control group, the invasion inhibition rate of cancer cells cultured with curcumin significantly increased, and a high concentration caused a high invasion inhibition rate. This means that the invasion of endometrial cancer may be inhibited by curcumin, and its effect size may be related to its concentration. In the knockdown of MMP-2, it was observed in the low concentration group that cell invasion inhibition rate further increased; while cell invasion rate decreased after the overexpression of MMP-2. The above results suggest that MMP-2 may play an important role in the inhibition of curcumin on endometrial cancer cell invasion.

This investigation still has some limitations. The concentration of curcumin included in the present study was relatively low, merely a single type of endometrial cancer was used, the study failed to conduct a subgroup analysis. At the same

time, it remains to be determined whether MMP-2 gene expression levels can completely pass through the MMP-2 protein and mRNA. Furthermore, the presence of other MMP-2 signaling pathways remains unclear, and the effect of curcumin and MMP-2 on the infiltration of endometrial carcinoma was not discussed. In future trials, the investigator would undertake the segmentation of curcumin concentrations with different types of endometrial cancer cells, in order to explore the possible mechanism of curcumin on the proliferation, metastasis, invasion, and infiltration of endometrial carcinoma, and further verify our conclusions.

Conclusion

We found that curcumin inhibits cancer cells to proliferate into a potential target, which may be due to MMP-2, and its concentration may be related to the intensity of MMP-2. As an object that inhibits the invasion of endometrial cancer in the study, it has potential clinical value.

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