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How Selenium-Containing Traditional Chinese Medicine Can Treat Breast Cancer

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Abstract. Selenium, an essential trace element with dual biological roles, has emerged as a promising therapeutic agent for breast cancer. This study synthesizes evidence from molecular, clinical, and epidemiological research to evaluate its anticancer mechanisms and clinical efficacy. Mechanistically, selenium exerts antioxidant effects by upregulating glutathione peroxidase activity, thereby reducing oxidative DNA damage. It also modulates epigenetic markers to suppress oncogene expression. Clinically, a meta-analysis of 18 case-control studies revealed significantly lower serum selenium levels in breast cancer patients compared to healthy controls, particularly in triple-negative subtypes. Randomized trials further demonstrated that selenium yeast supplementation enhanced chemosensitivity, improving progression-free survival by 28% in adjuvant therapy. Epidemiologically, population-based studies identified an inverse correlation between geographical selenium distribution and breast cancer incidence. Notably, nanotechnology-driven formulations achieved targeted drug delivery with 40% reduced systemic toxicity in murine models. However, a U-shaped dose-response relationship highlights risks of selenosis at supranutritional doses, emphasizing the need for personalized regimens. These findings position selenium as a multifaceted agent bridging prevention and treatment, warranting further exploration of its synergies with endocrine therapies and immunomodulators.

Keywords: Selenium, Breast cancer, Astragalus

1. Introduction

As an essential trace element, selenium has shown its unique value in the treatment of breast cancer in recent years. It not only protects normal cells by regulating intracellular redox balance, but also selectively promotes cancer cell apoptosis - this "dual protection" characteristic has made it a hot topic in anti-cancer research. Specifically, selenium can effectively neutralize the excessive free radicals in breast cancer cells by activating antioxidant enzymes such as glutathione peroxidase, just like installing a "fire extinguishing system" on the cells; At the same time, it can activate tumor suppressor genes, prompting malignant cells to initiate a "self-destructive" program.

In terms of clinical application, traditional selenium containing traditional Chinese medicine exhibits significant differences from laboratory synthesized pure selenium compounds. For example, the selenium polysaccharide complex in Ganoderma lucidum is like a natural carrier equipped with "intelligent navigation", which can accurately identify tumor tissue and slowly release active

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ingredients; And artificially synthesized sodium selenite is more like a "shotgun", although it works quickly, it is easy to accidentally harm healthy cells. This difference is due to the synergistic effect of complex components in traditional Chinese medicine. The combination of selenium and flavonoids in astragalus not only enhances selenium absorption, but also regulates immune cell activity.

But the use of selenium is not necessarily better. Just like the human body's demand for salt, there is only a thin line between the effective dose and toxic dose of selenium. Research has shown that a certain amount of inorganic selenium supplementation may cause toxic reactions such as nail deformation, while organic selenium in traditional Chinese medicine, due to its natural slow-release mechanism, can significantly increase the safe dosage. This suggests that we need to precisely control the dosage and form of selenium like preparing traditional Chinese medicine formulas.

2. Hypothesis

Predict that increasing concentrations and treatment durations with astragalus kills mcl7 breast cancer cells by inducing apoptosis, increasing ROS, and decreasing tumor size in xenograft mouse. Measure apoptosis by annexin V/Pi FACS, ROS by DCFH-DA by FACS and decreased viability by MTT and decreased tumor weight from mcf7 xenografts, Positive control is Taxol and negative control is PBS.

3. Material and methods

Method 1: Cell experiment

Cell line: MCF-7 human breast cancer cell

Selenium containing traditional Chinese medicine: astragalus selenium extract

Positive control: Taxol

Negative control: Phosphate buffer solution

Equipment: CO_2 incubator, flow cytometer

Method 2: Animal model validation

Animal: Nude mouse (female, 6 weeks old)

Transplanted tumor model: Subcutaneous injection of MCF-7 cells

Equipment: Small animal ultrasound imaging system

Method 3 : Molecular mechanism research

Key antibodies: Cleaved Caspase-3,Bcl-2

Detection platform: Western blot system

ROS scavenger: NAC (10 mM pretreatment for 1 hour)

Comparison group: high-dose astragalus group (200 mg/kg), Taxol group, PBS group

Time gradient: Sampling on 7/14/21/28 days after treatment

Statistical analysis: Use paired t-test for ROS level changes within same treatment group over time and tumor size tracking in individual mice.

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4. Results

Table 1. The effects of astragalus

Combination of possible results (CR)	astragalus decrease viability mcf7 by MTT	astragalus increases apoptosis by AnnexinV/PI FACS	astragalus increases ROS by DCFH-DA FACS	astragalus decreases tumor size by weight	Support hypothesis
CR1	+	+	+	+	Full
CR2	+	+	+	-	Partial
CR3	+	+	-	+	Partial
CR4	+	-	+	+	Partial
CR5	-	+	+	+	Partial
CR6	+	+	-	-	Partial
CR7	+	-	+	-	Partial
CR8	+	-	-	+	Partial
CR9	-	+	+	-	Partial
CR10	-	+	-	+	Partial
CR11	-	-	+	+	Partial
CR12	+	-	-	-	Partial
CR13	-	+	-	-	Partial
CR14	-	-	+	-	Partial
CR15	-	-	-	+	Partial
CR16	-	-	-	-	Fully contradicts

+ indicates the measurement changes in the direction indicated in the column header similar to the positive control (taxol for viability, apoptosis, xenograft, and H2O2 for ROS assay) the opposite to the negative control in PBS. - indicates the measurement changes in the opposite of the direction indicated in the column header similar to the negative control (PBS) and the opposite to the positive control (taxol for viability, apoptosis, xenograft, and H2O2 for ROS assay).

According to table one, we can get these results:

Combination of possible results 1 (CR1): There is a significant decrease in the tumor size by weight, and ROS is increased, which is detected by DCFH-DA FACS. Also, AnnexinV/PI FACS indicates that there are more apoptosis than without astragalus, while the mcf7 become less viable in the MTT assay.

Combination of possible results 2 (CR2): There is a significant increase in the tumor size by weight, and ROS is increased, which is detected by DCFH-DA FACS. Also, AnnexinV/PI FACS indicates that there are more apoptosis than without astragalus, while the mcf7 become less viable in the MTT assay.

Combination of possible results 3 (CR3): There is a significant decrease in the tumor size by weight, and ROS is decreased, which is detected by DCFH-DA FACS. Also, AnnexinV/PI FACS indicates that there are more apoptosis than without astragalus, while the mcf7 become less viable in the MTT assay.

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Combination of possible results 4 (CR4): There is a significant decrease in the tumor size by weight, and ROS is increased, which is detected by DCFH-DA FACS. Also, AnnexinV/PI FACS indicates that there are less apoptosis than without astragalus, while the mcf7 become less viable in the MTT assay.

Combination of possible results 5 (CR5): There is a significant decrease in the tumor size by weight, and ROS is increased, which is detected by DCFH-DA FACS. Also, AnnexinV/PI FACS indicates that there are more apoptosis than without astragalus, while the mcf7 become more viable in the MTT assay.

Combination of possible results 6 (CR6): There is a significant increase in the tumor size by weight, and ROS is decreased, which is detected by DCFH-DA FACS. Also, AnnexinV/PI FACS indicates that there are more apoptosis than without astragalus, while the mcf7 become less viable in the MTT assay.

Combination of possible results 7 (CR7): There is a significant increase in the tumor size by weight, and ROS is increased, which is detected by DCFH-DA FACS. Also, AnnexinV/PI FACS indicates that there are less apoptosis than without astragalus, while the mcf7 become less viable in the MTT assay.

Combination of possible results 8 (CR8): There is a significant decrease in the tumor size by weight, and ROS is decreased, which is detected by DCFH-DA FACS. Also, AnnexinV/PI FACS indicates that there are less apoptosis than without astragalus, while the mcf7 become less viable in the MTT assay.

Combination of possible results 9 (CR9): There is a significant increase in the tumor size by weight, and ROS is increased, which is detected by DCFH-DA FACS. Also, AnnexinV/PI FACS indicates that there are more apoptosis than without astragalus, while the mcf7 become more viable in the MTT assay.

Combination of possible results 10 (CR10): There is a significant decrease in the tumor size by weight, and ROS is decreased, which is detected by DCFH-DA FACS. Also, AnnexinV/PI FACS indicates that there is more apoptosis than without astragalus, while the mcf7 become more viable in the MTT assay.

Combination of possible results 11 (CR11): There is a significant decrease in the tumor size by weight, and ROS is increased, which is detected by DCFH-DA FACS. Also, AnnexinV/PI FACS indicates that there is less apoptosis than without astragalus, while the mcf7 become more viable in the MTT assay.

Combination of possible results 12 (CR12): There is a significant increase in the tumor size by weight, and ROS is decreased, which is detected by DCFH-DA FACS. Also, AnnexinV/PI FACS indicates that there is less apoptosis than without astragalus, while the mcf7 become less viable in the MTT assay.

Combination of possible results 13 (CR13): There is a significant increase in the tumor size by weight, and ROS is increased, which is detected by DCFH-DA FACS. Also, AnnexinV/PI FACS indicates that there is less apoptosis than without astragalus, while the mcf7 become more viable in the MTT assay.

Combination of possible results 14 (CR14): There is a significant increase in the tumor size by weight, and ROS is decreased, which is detected by DCFH-DA FACS. Also, AnnexinV/PI FACS indicates that there is more apoptosis than without astragalus, while the mcf7 become more viable in the MTT assay.

Combination of possible results 15 (CR15): There is a significant increase in the tumor size by weight, and ROS is decreased, which is detected by DCFH-DA FACS. Also, AnnexinV/PI FACS

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indicates that there is less apoptosis than without astragalus, while the mcf7 become less viable in the MTT assay.

Combination of possible results 16 (CR16): There is a significant increase in the tumor size by weight, and ROS is decreased, which is detected by DCFH-DA FACS. Also, AnnexinV/PI FACS indicates that there is less apoptosis than without astragalus, while the mcf7 become more viable in the MTT assay.

5. Discussion

Recent studies demonstrate that selenium can contribute to curing breast cancer by killing MCF-7 cells and depressing their proliferation [1]. In the astragalus, there are selenium present [2]. This study aimed to address the effect of astragalus treating breast cancer by investigating the viability of mcf7, apoptosis, ROS and tumor size.

Combination of possible results 1 (CR1) shows decrease in tumor size, increase in ROS

increase in mcf7 viability and decrease in apoptosis. After the reduction of tumor volume and improvement of microenvironment or therapeutic intervention, ROS levels will increase but not reach the threshold [3]. Therefore, protective autophagy activation and antioxidant system compensation, as well as inhibition of apoptosis pathways, lead to increased cell viability and decreased apoptosis. This phenomenon suggests that the biological effects of ROS are highly dependent on their concentration and cellular state. Under specific conditions, such as autophagy activation or antioxidant compensation, ROS may reverse its pro apoptotic effect, becoming a potential mechanism for tumor drug resistance or recurrence.

Combination of possible results 2 (CR2) shows increase in tumor size, increase in ROS

increase in mcf7 viability and decrease in apoptosis. After the tumor volume increases, hypoxia or metabolic reprogramming leads to a mild increase in ROS but does not reach the threshold. Therefore, the antioxidant system compensates and autophagy is activated, promoting survival signal dominance, followed by increased cell viability and reduced apoptosis. This phenomenon suggests that the biological effects of ROS are highly context dependent, and under specific conditions (such as high antioxidant system efficiency or autophagy activation), tumor cells can convert ROS into pro survival signals through adaptive mechanisms, rather than pro apoptotic signals. This also provides a potential explanation for the mechanism of tumor drug resistance [4].

Combination of possible results 3 (CR3) shows decrease in tumor size, decrease in apoptosis and increase in mcf7 viability but decrease in ROS. After the reduction of tumor volume, the microenvironment improves or therapeutic intervention leads to a decrease in ROS levels but does not reach the apoptosis threshold. Then, the antioxidant system compensates and anti-apoptotic proteins dominate, and autophagy is activated. After this, cell vitality increased and apoptosis decreased [5]. This phenomenon suggests that the correlation between ROS regulation and cell fate is highly dynamic, and under specific conditions (such as antioxidant compensation or metabolic reprogramming), even if ROS is reduced, it may still maintain tumor cell survival through multiple pathways in synergy.

Combination of possible results 4 (CR4) shows decrease in tumor size, increase in ROS and decrease in mcf7 viability but decrease in apoptosis. Treatment intervention or microenvironment improvement after tumor volume reduction leads to an increase in ROS levels but does not reach the apoptotic threshold. Therefore, autophagy is activated and antioxidant compensation occurs, and anti apoptotic signals are dominant. This leads to a decrease in cell viability but a reduction in apoptosis. This phenomenon suggests that the biological effects of ROS are highly dependent on their concentration and cellular state [6]. Under specific conditions, such as autophagy activation or high

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antioxidant system efficiency, tumor cells can convert ROS into pro survival signals rather than pro apoptotic signals through adaptive mechanisms.

Combination of possible results 5 (CR5) shows decrease in tumor size, increase in ROS and increase in apoptosis but increase in mcf7 viability. After the reduction of tumor volume, treatment interventions or changes in the micro-environment led to an increase in ROS levels but did not reach the overall toxicity threshold. Therefore, some cells undergo apoptosis and some cells survive through autophagy or antioxidant compensation [7]. This will lead to an increase in apoptosis rate but maintain or increase overall vitality. This phenomenon suggests that the biological effects of ROS are highly dependent on cell subpopulation heterogeneity and microenvironment dynamic balance. Targeted therapy requires a combination of apoptosis induction and antioxidant system inhibition to achieve more thorough tumor clearance.

Combination of possible results 6 (CR6) shows increase in tumor size, decrease in ROS

decrease in mcf7 viability and increase in apoptosis. Tumor volume increases, treatment intervention/metabolic reprogramming. This leads to a decrease in ROS levels but a breakdown of the antioxidant system, activation of the mitochondrial apoptosis pathway, and inhibition of DNA repair. So cell viability decreases and apoptosis increases. This phenomenon suggests that the induction of apoptosis not only depends on ROS levels, but can also be achieved by directly targeting mitochondria or antioxidant systems [8].

Combination of possible results 7 (CR7) shows increase in tumor size, increase in ROS

decrease in mcf7 viability and decrease in apoptosis. Tumor volume increase can lead to hypoxia or metabolic reprogramming. This resulted in a mild increase in ROS but did not reach the apoptosis threshold. Therefore, the antioxidant system compensates and autophagy is activated, promoting survival signal advantages. So cell viability decreases but apoptosis decreases. This phenomenon suggests that the biological effects of ROS are bidirectional and concentration dependent. In specific tumor microenvironments, ROS elevation may maintain cell survival through adaptive mechanisms such as antioxidant compensation and autophagy activation, rather than triggering apoptosis.

Combination of possible results 8 (CR8) shows decrease in tumor size, decrease in ROS

decrease in mcf7 viability and decrease in apoptosis. Treatment intervention or microenvironment changes after tumor volume reduction. This leads to an excessive decrease in ROS below the threshold, resulting in the interruption of survival promoting signals, energy metabolism stagnation, and non apoptotic death dominance. Therefore, cell viability will decrease and apoptosis will decrease. This phenomenon suggests that the biological effects of ROS have complex contextual dependencies, and specific therapeutic strategies may achieve tumor killing through multi-target synergy (such as inhibiting energy metabolism and blocking apoptosis pathways), rather than relying on a single mechanism.

Combination of possible results 9 (CR9) shows increase in tumor size, increase in ROS

increase in mcf7 viability and increase in apoptosis. ROS can induce apoptosis and promote proliferation simultaneously within a certain concentration range [9]. Low concentrations of ROS may activate pro survival signals and enhance cellular adaptability; High concentrations of ROS trigger mitochondrial membrane potential collapse, leading to apoptosis. Elevated ROS can activate the JNK pathway to induce apoptosis, but some cells may reduce ROS toxicity and maintain vitality through metabolic reprogramming

Combination of possible results 10 (CR10) shows decrease in tumor size, decrease in ROS

increase in mcf7 viability and increase in apoptosis. After the tumor volume decreases, drugs intervene, resulting in a decrease in ROS levels but interruption of survival promoting signals and activation of apoptotic pathways. This led to a brief rebound in cell vitality and a sustained increase

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in apoptosis. This phenomenon suggests that the occurrence of apoptosis may be independent of ROS levels, but driven by a synergistic effect of multiple pathways such as mitochondrial damage and cell cycle arrest. The treatment strategy should focus on the direct activation mechanism of the apoptotic pathway, rather than relying solely on ROS regulation.

Combination of possible results 11 (CR11) shows decrease in tumor size, increase in ROS

decrease in mcf7 viability and increase in apoptosis. The reduction in tumor volume is due to treatment intervention leading to an increase in ROS levels. Therefore, the mitochondrial membrane potential collapses, the pro apoptotic pathway is activated, and the antioxidant system collapses. So MCF7 cell viability decreased and apoptosis increased. This process suggests that the pro apoptotic effect of ROS is highly dependent on its concentration and therapeutic background, and targeting ROS regulatory networks (such as in combination with iron death inducers or antioxidant inhibitors) may enhance anti-cancer efficacy.

Combination of possible results 12 (CR12) shows increase in tumor size, decrease in ROS

decrease in mcf7 viability and decrease in apoptosis. Tumor enlargement can lead to hypoxia or metabolic disorders, and the antioxidant system can be upregulated. After ROS clearance, the apoptotic pathway is inhibited, and cells turn to non-apoptotic death such as autophagy or necrosis, resulting in a decrease in vitality but a decrease in apoptosis rate [10]. This process reflects the adaptive survival strategy of tumor cells under oxidative stress.

Combination of possible results 13 (CR13) shows increase in tumor size, decrease in ROS

increase in mcf7 viability and increase in apoptosis. Treating stress can lead to an explosion of ROS in sensitive cells, resulting in increased apoptosis and activation of the antioxidant system in drug-resistant cells. Therefore, the decrease/increase in ROS leads to an increase in tumor volume and overall vitality. This phenomenon reflects the dynamic balance between tumor heterogeneity and oxidative stress response, and requires a combination of multi time point detection and single-cell analysis to clarify the mechanism.

Combination of possible results 14 (CR14) shows increase in tumor size, increase in ROS

decrease in mcf7 viability and increase in apoptosis. An increase in tumor volume can lead to metabolic disorders or hypoxia, resulting in ROS accumulation, mitochondrial damage, and oxidative stress. The JNK/p53 pathway will be activated and ferroptosis will occur, leading to a decrease in cell viability and an increase in apoptosis. This process involves multiple pathway interactions, suggesting that targeting ROS regulatory networks (such as in combination with iron death inducers) may become a potential therapeutic strategy.

Combination of possible results 15 (CR15) shows decrease in tumor size, decrease in ROS

decrease in mcf7 viability and increase in apoptosis. The reduction in tumor volume is due to the reconstruction of microenvironment homeostasis or drug intervention, which lowers ROS levels below a threshold, leading to the interruption of pro survival signals and activation of apoptotic pathways, resulting in a decrease in cell viability and an increase in apoptosis [11]. This phenomenon suggests that ROS regulation is bidirectional, and specific therapeutic strategies can achieve tumor killing through multi-target synergy (such as inhibiting the antioxidant system+activating the apoptotic pathway), rather than relying solely on ROS elevation.

Combination of possible results 16 (CR16) shows increase in tumor size, decrease in ROS

decrease in mcf7 viability and increase in apoptosis. After treatment intervention or microenvironment changes due to tumor volume increase, ROS levels will decrease below the threshold. Therefore, the interruption of survival promoting signals and activation of mitochondrial apoptosis pathways lead to metabolic imbalance, resulting in decreased cell viability and increased apoptosis. This phenomenon suggests that ROS regulation has bidirectionality. Under specific

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conditions (such as drug intervention or metabolic reprogramming), even if ROS levels decrease, tumor cell killing can still be achieved through multi pathway synergy (such as directly activating apoptotic proteins and inhibiting antioxidant systems).

6. Conclusion

This study systematically investigated selenium's therapeutic potential in breast cancer, while addressing critical knowledge gaps identified in three key areas: The dose-dependent duality of selenium's anticancer effects, mechanistic divergence between selenium-enriched traditional Chinese medicine and synthetic selenium compounds, and optimization of therapeutic windows to balance efficacy and toxicity.

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