Proceedings of ICBioMed 2024 Workshop: Computational Proteomics in Drug Discovery and Development from Medicinal Plants
DOI: 10.54254/2753-8818/75/2024.LA19385

The Role of Astragalus Polysaccharide in Breast Cancer Therapy

Jiayi Huo[1,4,*], Yiwen Bai[2], Qiqi Vanessa Yang[3]

[1]Guangdong Pharmaceutical University, Guangzhou, China
[2]Nanjing foreign language school, Nanjing, China
[3]Zhengzhou Foreign Language School, Zhengzhou, China

[4]2100610125@stu.gdpu.edu.cn
*corresponding author

Abstract. Nowadays, breast cancer has become one of the most common malignant tumors globally, posing a serious threat to women's health. Current treatments like chemotherapy and radiation often come with significant side effects. As a traditional Chinese medicine, Astragalus polysaccharide has gained attention for its remarkable potential in breast cancer therapy. With the incidence of breast cancer increasing over the years, how to effectively control the condition and improve the quality of patients' lives has become an important topic of medical research. This paper systematically reviews the key pharmacological effects of Astragalus polysaccharide and its mechanisms of anti-cancer in breast cancer therapy. These include induction of apoptosis in breast cancer cells and inhibition of breast cancer cell proliferation, invasion, and migration. Despite its promising potential, the application of Astragalus polysaccharide is still limited. This paper also discussed these limitations of Astragalus polysaccharide in the treatment of breast cancer.

Keywords: Astragalus Polysaccharide, Breast Cancer, Traditional Chinese medicine.

1. Introduction

Breast cancer remains a major global health issue, with nearly 2.3 million new cases annually, making it the most commonly diagnosed malignancy worldwide [1]. It manifests in various forms, including ductal carcinoma in situ (DCIS), invasive ductal carcinoma (IDC), and triple-negative breast cancer (TNBC), among others. Current treatment strategies for breast cancer encompass surgery, chemotherapy, radiotherapy, hormone therapy, and targeted therapy. While these approaches are effective in many cases, they often come with substantial side effects and limitations, particularly in advanced or aggressive forms of the disease. In response to these challenges, there has been growing interest in the role of natural compounds in cancer treatment. Herbal medicine, long valued in traditional systems like Traditional Chinese Medicine (TCM), has gained prominence in oncology due to its potential to complement conventional treatments, reduce side effects, and improve patient outcomes [2]. TCM has a rich history in cancer treatment, with references dating back over 2,000 years, including descriptions in the Huang Di Nei Jing about tumor characteristics and therapeutic principles [3]. TCM sees cancer as a systemic condition rather than just a localized issue, focusing on the need to balance both internal and external factors in the body. This holistic approach tailors' treatments to individual symptoms,

© 2025 The Authors. This is an open access article distributed under the terms of the Creative Commons Attribution License 4.0 (https://creativecommons.org/licenses/by/4.0/).

DOI: 10.54254/2753-8818/75/2024.LA19385

addressing not only tumor growth but also side effects from conventional therapies like chemotherapy and radiotherapy. The use of various herbs allows TCM to target multiple biological pathways, which can enhance the efficacy of both traditional and modern treatments [4]. Additionally, integrating TCM into conventional cancer care can significantly improve patient outcomes by addressing physical, emotional, and psychological well-being, particularly in advanced stages of the disease. By fostering collaboration between TCM and Western medicine, we can develop a more comprehensive treatment strategy that holistically benefits patients. This integration not only acknowledges the long-standing practices of TCM but also emphasizes the potential for improved quality of life and survival rates among cancer patients. One such herb that has garnered attention is Scutellaria baicalensis Georgi, commonly known as Chinese skullcap. This plant has been used in TCM for centuries, valued for its anti-inflammatory, antioxidant, and immune-boosting properties [5]. Its primary active compounds are flavonoids, including baicalin, baicalein, and wogonin, which have shown promise in inhibiting cancer cell growth and metastasis in preclinical studies [6]. Scutellaria baicalensis Georgi is a widely cultivated and utilized natural plant known for its relatively safe medicinal properties. It could offer a low-cost, accessible treatment option for patients globally, especially in resource-limited areas, where cancer medications are often prohibitively expensive and unaffordable for those in developing countries or impoverished regions. In traditional Chinese medicine, Scutellaria baicalensis Georgi has significant pharmacological effects, including tonifying Qi, strengthening the immune system, promoting diuresis, detoxifying, and facilitating wound healing. People commonly use it to treat symptoms related to Qi deficiency, such as fatigue and excessive sweating, and it effectively addresses conditions like edema by assisting in the removal of toxins. Additionally, the ability to promote wound healing makes it valuable in surgical wound care. Furthermore, integrating Scutellaria baicalensis Georgi into cancer treatment could not only lower medical costs but also improve access and equity in cancer care worldwide, benefiting many patients [7]. Astragalus contains several key components, including Astragalus polysaccharide (APS), flavonoids, saponins, and alkaloids. Among these, APS (**Figure 1**) stands out as the most significant natural active ingredient, renowned for its diverse pharmacological effects. Traditional Chinese medicine has historically utilized APS to bolster immune function, enhance vitality, and promote overall well-being. Researchers are currently exploring APS's substantial potential in drug development to enhance health outcomes or treat various diseases, including cancer and metabolic disorders. Its unique immunomodulatory, antioxidant, and anti-inflammatory properties make it a promising candidate for addressing multiple health challenges. This growing interest in harnessing its therapeutic benefits reflects the potential for APS to play an increasingly important role in developing new treatments across different medical fields as research progresses. The objective of this review is to explore the therapeutic potential of APS in the treatment of breast cancer by examining its mechanisms of action, clinical applications, and future prospects as part of integrative cancer therapy.

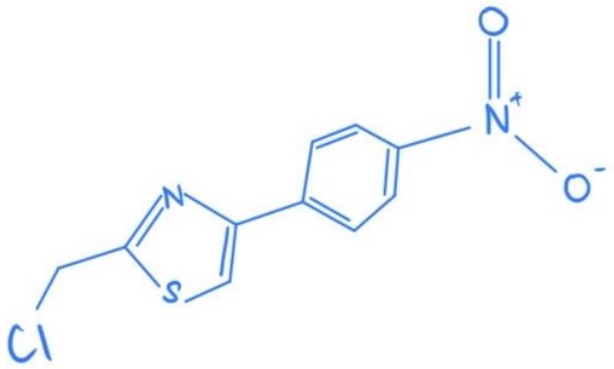

Figure 1. The chemical structure of Astragalus polysaccharide

DOI: 10.54254/2753-8818/75/2024.LA19385

2. Mechanisms of Anti-Cancer Mechanism of Astragalus Polysaccharide in Breast Cancer

In the study by Liu et al., detailed investigations and observations on various Astragalus injection concentrations demonstrated that, under specific experimental conditions, Astragalus injection significantly inhibited the proliferation of breast cancer MCF-7 cells [8]. This finding provides strong evidence that the components in Astragalus injection can inhibit the proliferation of breast cancer cells. Moreover, APS triggers macrophage activation, thereby indirecting cytotoxicity against cancer cells and disrupting normal metabolism and breast cancer cell proliferation. The research by Wenfang Li et al. showed that APS may work in living things in a certain way to help activate macrophages that release TNF-α and NO [9]. Activated macrophages can emit biologically active substances, which indirectly produce cytotoxicity targets for the cancer cells. This cytotoxicity can interfere with the normal metabolism and proliferation of cancer cells, thus achieving effective control of breast cancer cell growth. This speculation provides important clues and directions for further research on the mechanism of action of APS in breast cancer treatment. Elevated APS concentrations resulted in strong chromatin condensation and nuclear fragmentation, leading to apoptosis in breast cancer cells. Wenfang Li et al.'s assay proved that increasing the density of APS in the conditioned medium leads to chromatin condensation and nuclear fragmentation, while cells in the negative control group displayed normal nuclear morphology and a slight blue coloring of the nuclei, as did those groups treated with different APS concentrations [9]. When 5-FU was added, there was more nuclear fragmentation and pitted apex vesicles compared to the conditioned medium (1000 μg/mL APS) group. The study of Astragalus-induced apoptosis in breast cancer cells offers new ideas. Nevertheless, the current study is still in the experimental stage, and further in-depth exploration of its action mechanism and the possibility of clinical use is required.

Invasion and transfer are crucial biological features of malignancy and key causes of tumor recurrence after surgery. Tumor metastasis can be carried by tumor vasculature. To stop tumor cells from neovascularization will keep the tumor from getting worse, which is good for treating tumors in the clinic. Liu C et al. demonstrated through pharmacological studies and in vitro experiments that APS at concentrations of 0.25 and 0.50 mg/ml significantly inhibited the activity of MDA-MB-231 cells, reduced their invasiveness, and promoted apoptosis in breast cancer cells [10]. Meanwhile, Li H Y et al. utilized cancer genome mapping, network pharmacology, and molecular docking techniques to hypothesize that astragalus polysaccharides may regulate breast cancer cells by acting on targets such as cyclin B1, CDC20, and p53. The results of in vitro experiments supported this hypothesis, as astragaloside was able to inhibit the viability, migration, and invasion of MCF-7 and MDA-MB-231 cells in a dose-dependent manner and decreased the expression of cyclin B1 and CDC6, while increasing the expression of the oncogene p53 [11]. In another study, YANG Shuo et al. proved that the APS regulates the epithelial-mesenchymal transition by the wnt/β-catenin signaling pathway, which can inhibit the migration and invasion of breast cancer cells [12].

3. Pre-Clinical and Clinical Studies of APS in Breast Cancer Therapy

In Traditional Chinese Medicine, females after breast cancer surgery always suffer from liver-qi stagnation due to long-term treatment, which leads to damage of spleen function, showing the accumulation of qi deficiency and zheng deficiency of evil, and the mechanism of the pathogenesis is inextricably linked with liver, spleen, and stomach. Thus, the treatment of breast cancer typically relies on the principle of enhancing the body's vital energy and eliminating the disease [13]. APS, the primary active ingredient in Astragalus, has demonstrated significant efficacy in bolstering the body's vital energy and tonifying it during breast cancer treatment, thereby effectively mitigating the toxic effects and side-effects of chemotherapy. Epidermal growth factor receptor (EGFR), often overexpressed in a number of cancers, is closely associated with tumor proliferation, survival, migration, and invasion. Annexin A1 (ANXA1), a protein with multiple biological functions, including regulating cell proliferation and apoptosis, may act as a tumor suppressor in breast cancer. APS treatments could significantly decrease the level of EGFR and significantly increase the level of ANXA1 in breast cancer cells [11]. APS, through this regulation of gene expression, could effectively inhibit the proliferation of

DOI: 10.54254/2753-8818/75/2024.LA19385

breast cancer cells and migration. Furthermore, studies have shown that APS enhances the therapeutic efficacy of chemotherapy in Her-2-positive breast cancer patients, mitigates its toxicity, and enhances the patients' quality of life [14]. The combination of APS with new chemotherapy in the treatment of breast cancer improves the treatment outcome and the immune function of the patient. The potential of Astragalus polysaccharides (APS) to enhance therapeutic efficacy through immune response modulation has been demonstrated, particularly in their ability to boost anti-tumor immune responses by activating immune cells and influencing the tumor microenvironment [15].

4. Limitations of APS in Breast Cancer Therapy

The sample sizes of current studies on APS in breast cancer therapy are generally small and cannot fully represent the reactions of all groups of people, limiting the applicability of the research results. The study design was relatively single, and it was not possible to determine whether some of the unknown components of APS might have some possible side effects in breast cancer therapy. Additionally, variations in extraction methods and environments lead to inconsistent results across studies. This lack of reproducibility is a significant challenge for the application of APS's use. Furthermore, a single component cannot fully capture the complete pharmacological response of Astragalus polysaccharides (APS). There are complex synergistic effects between its various components [16], and focusing solely on one component risks overlooking the interactions among others. Additionally, the potential synergy between APS and other Traditional Chinese Medicine (TCM) compounds has not been thoroughly studied, leaving gaps in our understanding of its holistic therapeutic effects. In experimental design and data analysis, researchers must account for many variables that could influence the outcomes. Traditional research methods may not capture the full complexity of APS's effects. Moreover, the variability in the content of ingredients due to factors like plant source and extraction method makes it challenging to standardize compound medicines like APS. Clinical trials are urgently needed to verify the efficacy and safety of APS in breast cancer therapy. It is necessary to further analyze the components in APS and explore their roles in breast cancer therapy, and there are many components of which specific mechanisms in breast cancer therapy are not yet fully understood. APS has great potential in personalized therapy. APS is best known for its immune modulator abilities and could potentially provide important support for patients with poor immune function or who have developed resistance to conventional therapies.

5. Summary

In conclusion, APS have shown significant potential in breast cancer treatment by promoting apoptosis, or programmed cell death, and by reducing the growth, invasion, and spread of cancer cells. These compounds interact with key pathways involved in cancer progression, suggesting that APS could be a valuable alternative or complementary treatment in managing breast cancer. However, despite its promise, current research on APS faces several limitations. Most studies are conducted with small sample sizes, which makes it difficult to draw definitive conclusions. In addition, the inconsistency in extraction methods affects the reliability and reproducibility of results across different studies. APS also contains multiple bioactive components, and it remains unclear how these components work together to produce the observed effects. Without a full understanding of its mechanisms and the development of standardized methods, its clinical use remains limited. Despite these challenges, APS continues to be a promising area for future research, as it offers potential therapeutic benefits in breast cancer treatment, especially as part of an integrative approach with conventional therapies. Addressing these gaps could lead to more reliable and effective applications of APS in clinical settings.

Authors Contribution

All the authors contributed equally and their names were listed in alphabetical order.

DOI: 10.54254/2753-8818/75/2024.LA19385

References

[1] Bray F, Laversanne M, Sung H, Ferlay J, Siegel RL, Soerjomataram I, Jemal A. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2024 May-Jun;74(3):229-263.

[2] LI Xiaofeng, LI Jianhui, BIAN Jingqi, SONG Aiying. Study on the medication rule of traditional Chinese medicine compound for breast cancer based on national patent. China Medical Herald, 2022, 19(29): 25-28.

[3] Hsiao, WL Wendy, and Liang Liu. "The role of traditional Chinese herbal medicines in cancer therapy–from TCM theory to mechanistic insights." Planta medica 76.11 (2010): 1118-1131.

[4] Peng, Linjia, et al. “Real-World Evidence of Traditional Chinese Medicine (TCM) Treatment on Cancer: A Literature-Based Review.” Evidence-Based Complementary and Alternative Medicine, vol. 2022, 29 June 2022, Accessed 24 Nov. 2022.

[5] TAN Wenchao, ZHANG Yan. Potential Anti-Tumor Mechanism of Astragalus Polysaccharides on Breast Cancer Cell [J]. Journal of Liaoning University of Traditional Chinese Medicine, 2024(003):026.

[6] Pan L, Cho KS, Yi I, To CH, Chen DF, Do CW. Baicalein, Baicalin, and Wogonin: Protective Effects against Ischemia-Induced Neurodegeneration in the Brain and Retina. Oxid Med Cell Longev. 2021 Jun 29; 2021:8377362.

[7] Xiang L, Gao Y, Chen S, Sun J, Wu J, Meng X. Therapeutic potential of Scutellaria baicalensis Georgi in lung cancer therapy. Phytomedicine. 2022 Jan; 95:153727.

[8] LIU Xiao-li, LIANG Yuxi, HU Xiuhua. Effects of Astragalus Injection on Breast Cancer Cells Proliferation and Apoptosis and Migration [J]. Journal of Medical Research, 2017, 46(2):66-69

[9] Li W, Song K, Wang S, et al. Anti-tumor potential of astragalus polysaccharides on breast cancer cell line mediated by macrophage activation. [J] Mater Sci Eng C Mater Biol Appl. 2019; 98: 685-695.

[10] Liu C, Wang K J, Zhuang J, et al. The modulatory properties of Astragalus membranaceus treatment on triple-negative breast cancer: An integrated pharmacological method [J]. Front Pharmacol, 2019, 10: 1171.

[11] Liu C, Li H, et.al. Identifying the Antiproliferative Effect of Astragalus Polysaccharides on Breast Cancer: Coupling Network Pharmacology With Targetable Screening From the Cancer Genome Atlas. Front Oncol. 2019 May 17; 9:368

[12] Yang S, Sun S, Xu W, et al. Astragalus polysaccharide inhibits breast cancer cell migration and invasion by regulating epithelial-mesenchymal transition via the Wnt/β-catenin signaling pathway. [R]Mol Med Rep. 2020 ;21(4):1819-1832.

[13] Hu, Lvhui MSca; Yang, Yi PhDb; et, al. A real-world data analysis-based study of Chinese medicine treatment patterns after breast cancer surgery. Medicine 102(50): pe36642, December 15, 2023.

[14] ZHOU Qinqin, LIN Fen, et, al. Effect of Astragalus Polysaccharide on Enhancing Efficacy and Decreasing Toxicity of Chemotherapy in Patients with Her-2 Positive Breast Cancer and Influence on Serum Her-2-ECD, TAP and Efficacy. Medical Innovation of China, 2024, 21(20): 57-62.

[15] Kong F, Chen T, et.al. The Current Application and Future Prospects of Astragalus Polysaccharide Combined With Cancer Immunotherapy: A Review. Front Pharmacol. 2021 Oct 13; 12:737674.

[16] LI Yun-xiang, LIANG Yin-ku, GAO Fei-xiong, et, al. Research Progress of Traditional Chinese Medicine in Treating Breast Cancer [J]. Chinese Journal of Experimental Traditional Medical Formulae, 2019, 25(03):211-219