

Evaluating the Use of Astragalus in Breast Cancer Treatment

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RES 825: Medical Research Methodology

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December 6, 2024

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### **Abstract**

Each woman has a 12% lifetime risk of developing breast cancer, and among those, 10% are diagnosed with metastatic disease (breast cancer statistics, n.d.; DePolo, 2024). Even women diagnosed with stage 1–3 breast cancer face a 20–30% risk of recurrence as metastatic cancer (DePolo, 2024). Astragalus, a traditional herbal remedy, contains chemical constituents that researchers have shown to inhibit tumor growth, increase apoptosis (programmed cell death), and reduce metastasis (Cohen et al., 2022). Preclinical studies have demonstrated these effects in breast cancer cell lines and mouse models. This study proposes a randomized, double-blind, prospective cohort design to investigate whether daily intake of Astragalus improves clinical outcomes in women aged 45–65 diagnosed with metastatic breast cancer. Participants will receive Astragalus alongside standard treatments, and researchers will compare cancer progression, growth rate, and five-year survival between the intervention and control groups. If effective, Astragalus could serve as a non-toxic, accessible adjunct therapy for breast cancer patients. The study also aims to lay the groundwork for future research into the preventative potential of Astragalus in patients with early-stage invasive breast cancer. Ultimately, this research seeks to validate the role of Astragalus in breast oncology and expand integrative treatment options.

*Key words:* breast cancer, astragalus, metastatic

## Introduction

Women face a 12 percent chance of developing breast cancer, which accounts for 30 percent of all cancer diagnoses in women each year (breast cancer statistics, n.d.). Among those diagnosed, 10 percent have metastatic breast cancer. However, women diagnosed with stages 1 to 3 face a 20–30 percent risk of recurrence as metastatic breast cancer (DePolo, 2024).

Many patients turn to complementary medicine to help fight, prevent, or manage breast cancer, often seeking support from herbal therapies. Due to its long-standing history and clinical use, traditional Chinese medicine (TCM) offers a range of herbal remedies, including those with compounds known to enhance immunity, support overall health, and improve organ function—key elements in cancer treatment and prevention (Chen, 2024).

One promising herb in this field is Astragalus (Huang Qi). Practitioners of TCM have used Astragalus for over 2,000 years, as first recorded in *Shen Nong's Classic of Materia Medica*. Known as an adaptogen, Astragalus stimulates immune function—boosting both red and white blood cell production—supports liver and adrenal restoration, enhances digestion, replenishes energy, and helps regulate cellular metabolism (Holmes, 2007, pp. 286–288). Clinicians frequently use it to treat infections, support wound healing, and manage autoimmune conditions, adrenal insufficiency, liver disease, and metabolic disorders. Researchers have also documented its ability to increase leukocyte and platelet counts and reduce blood pressure (Denzler, 2015).

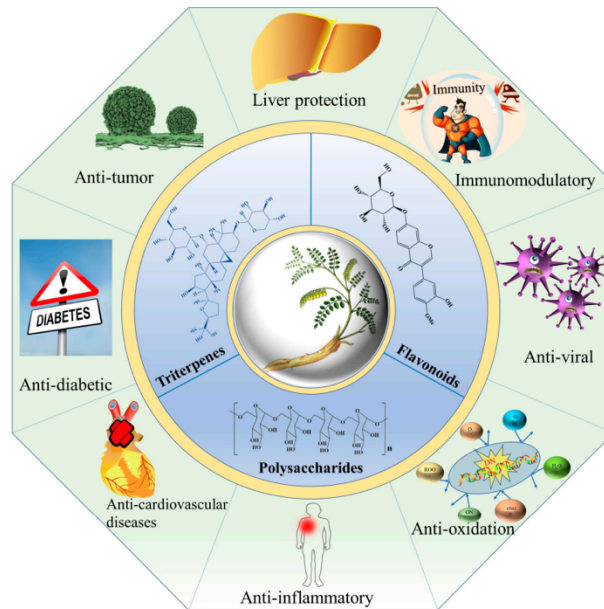
The inclusion of Astragalus in many traditional Chinese medicinal formulas further underscores its therapeutic potential, particularly in the context of cancer care.

Numerous studies have demonstrated how Astragalus influences the immune system. Brush et al. (2006) found that Astragalus, along with other herbs, enhanced immune response by increasing CD69 expression, an early marker of lymphocyte activation. Xu et al. (2023) reported that *Astragalus* polysaccharides stimulated the activity of macrophages, dendritic cells, natural killer cells, T lymphocytes, and B lymphocytes, while also inducing the expression of various cytokines and chemokines.

Researchers have studied this immune-modulating effect in the context of cancer. As early as 25 years ago, Sinclair (1998) identified Astragalus as an effective immune stimulant, making it a valuable adjunct in cancer therapy. More recently, Dong et al. (2023) illustrated the effects of triterpenes, flavonoids, and polysaccharides in Astragalus on the body (see Figure 1.1). These compounds play a beneficial role in cancer treatment, particularly in breast cancer, by supporting the immune system and enhancing the body's ability to respond to malignancy.

### **Figure 1.0**

Astragalus' effects on the body (Dong et al., 2023)



### Literature Review

Researchers have identified several significant cancer-fighting components of *Astragalus* in the literature, including polysaccharides (APS), triterpenes, and flavonoids. This review focuses on four key constituents: APS, saponins (a type of triterpene), and the flavonoids calycosin and formononetin. In addition, studies have shown that combining *Astragalus* with synergistic herb pairs enhances its therapeutic effects, playing an important role in breast cancer treatment.

### Astragalus Polysaccharides (APS)

Polysaccharides are macromolecules that play a vital role in supporting the body’s biological functions (Mohammed, 2021). Zhang et al. (2024) emphasized the significance of *Astragalus* polysaccharides (APS), referring to them as an

“indispensable ingredient of *Astragalus*.” In the context of breast cancer, researchers have demonstrated APS’s ability to inhibit tumor growth by stimulating the immune system (Li et al., 2018). Beyond immune activation, APS also suppresses tumor progression by promoting apoptosis (programmed cell death), reducing metastasis, and limiting cancer proliferation (Cohen et al., 2022).

He et al. (2024) reported that APS helps limit cancer spread by influencing immune cells, inducing cell death, triggering autophagy in cancer cells, and modifying the tumor microenvironment. Li et al. (2019) confirmed these effects in breast cancer cell lines. Additionally, Huang et al. (2019) found that APS, due to its anti-inflammatory properties, significantly improved quality of life in patients with Stage IV cancer.

Yang et al. (2020) showed that APS reduced the spread of invasive breast cancer in laboratory models. Their findings suggest that APS may inhibit the epithelial-mesenchymal transition (EMT), a key mechanism driving cancer metastasis and recurrence. Given that metastasis accounts for over 90% of breast cancer-related deaths (Benson, 2012), APS’s ability to disrupt this process underscores its clinical relevance.

APS also appears safe and well-tolerated when used alongside conventional treatments. It not only enhances therapeutic outcomes but also reduces side effects and mitigates chemotherapy toxicity (He et al., 2024). Tang and Tian (2024) reviewed studies demonstrating that combining *Astragalus* with chemotherapy in breast cancer cells led to synergistic effects, reduced drug resistance, and lower toxicity. Furthermore,

Dong et al. (2023) noted that APS may play a role in cancer prevention, expanding its potential utility beyond treatment.

### **Saponins**

Saponins, a type of triterpene found in *Astragalus*, represent another key component with cancer-fighting potential. Plant-based triterpenes are naturally occurring compounds that researchers have found effective against cancer, inflammation, oxidative stress, and a range of bacterial, fungal, and viral infections (Chudzick et al., 2015). Sheng et al. (2024) reported that "*Astragalus membranaceus* saponins exhibit significant anti-cancer effects through multiple mechanisms," particularly by inhibiting tumor cell proliferation, migration, and invasion, as well as by inducing apoptosis in both in vitro and in vivo studies (p. 1).

### **Flavonoids**

Flavonoids are naturally occurring components of herbs known to reduce gene mutations, lessen inflammation, and prevent cancer development (Panche et al., 2016). Two flavonoids of *Astragalus* in cancer research is formononetin and calycosin.

### ***Formononetin***

Researchers have identified formononetin as a promising compound in treating cancers that no longer respond to conventional drug therapies. Zhou et al. (2019) found that formononetin enhances the effectiveness of chemotherapy drugs, suggesting its potential as an adjunct treatment. Chang et al. (2024) further supported this, stating that formononetin should be incorporated into therapy for drug-resistant cancers, as it helps resensitize tumors to chemotherapy.

In the context of breast cancer, Song and Li (2022) noted that formononetin's anti-tumor effects may result from its ability to act on immune-related genes, indicating its therapeutic relevance in breast cancer treatment. Additionally, Chen et al. (2013) demonstrated that formononetin increases apoptosis and inhibits the growth of estrogen receptor-positive breast cancer cells.

### ***Calycosin***

Calycosin, another flavonoid found in *Astragalus*, has also demonstrated significant potential in cancer treatment. Researchers have shown that calycosin possesses anti-cancer, antioxidant, and anti-inflammatory properties, while also influencing estrogen regulation, blood function, and the nervous system (Gong et al., 2021). Tian et al. (2017) found that calycosin effectively inhibits the growth of both estrogen receptor-negative and estrogen receptor-positive breast cancer cells. Furthermore, Wu et al. (2019) reported that calycosin may serve as a therapeutic agent in treating aggressive forms of breast cancer.

## **Methodology**

### **Proposal**

From the literature review, studies show the cancer-inhibiting effects of Astragalus on tumor cell proliferation, migration, invasion, and induction of apoptosis" (Sheng et al., 2024, p. 1). Additional studies show the effects of Astragalus on breast cancer in mice (Zhu et al., 2015). However, none of the studies examined how Astragalus and constituents (triterpenes, polysaccharides, and flavonoids) affect breast cancer patients' long-term survival or recurrence rates. The research also addresses

very few studies done with humans. More research is needed to ascertain if Astragalus helps increase long-term survival rates of women diagnosed with metastatic breast cancer. This proposal recommends this study.

Research question: Do women between the ages of 45-65 diagnosed with metastatic breast cancer experience a slower spread, slower growth, and better long-term survival rates when taking an Astragalus decoction over 5 years?

### **Quantitative**

The purpose of this study is to test the theory that daily consumption of Astragalus can lower the 5-year mortality rate in women aged 45-65 diagnosed with stage 4 metastatic breast cancer. Independent variable is women aged 45-65. The dependent variable is the spread and growth of cancer plus the mortality rate within five years. The intervening variable, Astragalus, will be defined as 20g decocted and divided into three doses to be taken in the morning, mid-day, and nighttime.

### **Design**

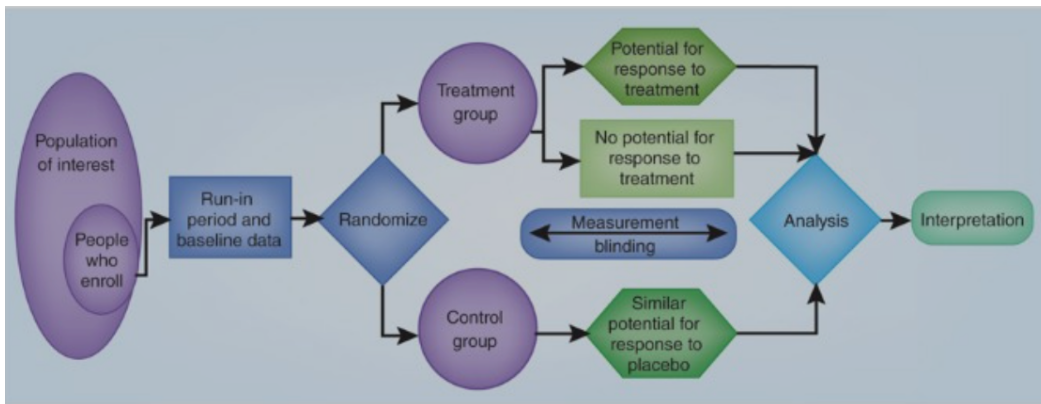
The null hypothesis: Women aged 45-65 diagnosed with metastatic breast cancer and taking Astragalus three times a day have the same risk of spread, growth, and long-term survival as those who do not take Astragalus. Alternative hypothesis: Long-term survival, spread, and cancer growth differ in those that take Astragalus.

To answer these questions, a prospective cohort study of randomly selected 385 female metastatic breast cancer patients between 45 and 65 years of age will be divided into two groups as shown in Figure 2.0. Group A receives 20g of decocted Astragalus divided into three daily doses. Group B is the control group and receives

20g of a decocted placebo. Statistical analysis will be conducted using the independent two-sided t-test with an alpha of 0.5 and beta of 0.2, and a potential pilot study will be conducted to determine the correct sample size that accounts for dropouts.

**Figure 2.0**

Randomized trial flow chart (Farrar, 2010).



Measurements for growth and spread are conducted with standardized measuring for precision. Growth and spread are measured by mammogram, ultrasound, bone scan, CT scan, PET scan, or MRI scan based on location of metastasis. The growth measurements of each cancer will be in numeric values, calculated as a percentage, and the means will be compared with the control group. Measurements of the number of new cancers (spread) will be gathered, and the means will be compared with those of the control group. The survival rate for the duration of the study (5 years) will also be calculated. These will also be compared with the control group. For instance, it is estimated that 168,000 women in the U.S. are living with metastatic breast cancer as of 2020, and only 31% of them will survive 5

years (Metastatic breast cancer, 2024). This can be compared to the study's control and treatment groups.

An additional survey could be added to this study. This would include having the patients answer questions about how they feel throughout the treatment while taking the herbal formula for a more subjective measurement of health. Qualitative results could rate how the recipient feels about the following aspects: positive outlook, tiredness/fatigue, symptom severity, and chemotherapy side effects. This research would have ordinal assignment (better, no difference, worse). The survey could be completed on day 1, halfway through the study, and at the end, with blinding for participants and researchers.

Hulley et al. (2013) describe the strengths of a randomized, double-blind trial as being able to identify cause and effect, reducing other variables that will distort the study, and keeping both participants and researchers unaware of who is in the study group and who is in the control group. The challenges to this type of study include the high cost and complexity, the difficulty in maintaining blinding, the potential for patient dropout, recruiting sufficient patients, overrepresentation of certain demographics, and concealing treatment versus control (Kang, 2008). This study could also have confounding variables, as each participant will receive the prescribed treatment by their oncologist. Therefore, patients will receive different medical treatments regardless of whether they are in the treatment group for herbs or the control. The use of Astragalus or the placebo will be in addition to any treatments they receive, including medications and chemotherapy. Those whose medications may harmfully interact with Astragalus will be excluded from the study.

### **Selection of Participants**

Potential participants are females between 45 and 65 years of age newly diagnosed with metastatic breast cancer in Maryland. Any results would be generalized to all women with stage 4 metastatic breast cancer. As stated above, this study will use a randomized, double-blind prospective cohort design. Participants will be selected via computer generated simple randomization (Kang et al., 2008).

Recruitment would involve asking those recently diagnosed with metastatic breast cancer in the Maryland cancer centers if they would be willing to participate in a new natural medicine research study on cancer treatment. Care should be taken not to overrepresent a certain demographic (Vaidyanathan, 2022). In addition, although little risk is associated with long-term use of Astragalus, those who are unlikely to adhere, follow up, or have an unacceptable risk would be excluded from the study.

### **Instrumentation**

All measurements on the size or spread of the tumors will be conducted according to the operations manual for the imaging equipment standardly used to view the type of metastatic cancer (i.e., ultrasound, MRI, CAT scan, PET scan, mammogram, or bone scan) to ensure precision. This operation manual will include standardization of the measurement method, specific guidelines and training for use, and ongoing calibration and repair of the equipment as standard in the hospital setting. All measurements will be repeated to reduce error and improve accuracy. The size and spread of tumors will be charted for each patient each year during their checkup or as

required by their oncologist for the routine medical check and, at the very least, at the beginning and end of the study. Deceased patients will also be noted.

Interviewers will be trained to reduce error and bias if the additional qualitative questionnaire is included in the study. The questionnaire can be filled out by the patient and sealed in an envelope without the patient's identifying information. This interview will be conducted every year. To negate any bias, researchers, those performing tests, and any interviewers will be blinded to which group the participant belongs (treatment vs. control), and they will be instructed not to discuss the research with the participant.

To ensure the study's validity, an oncologist will be consulted about the measurement parameters for each type of metastasis, including blood tests and other measures pertaining to the individual's metastatic cancer. This will be conducted during the planning phase prior to the onset of the study.

### **Proposed Analysis Procedures**

To analyze the data, the measurements of size and spread will be plotted and compared to the control group using an independent two-sample t-test. Survival rates would be statistically analyzed in a similar fashion. A statistical analysis will be conducted for those who discontinued treatment or dropped out. Researchers will use a “per-protocol” analysis to include only participants who adhered to the protocol and an “as-treated” analysis to include only participants who adhered to the assigned intervention.

### **Potential Limitations**

Another potential issue with this design, other than those listed above, is the length of study. Not only will this make the study time-consuming and expensive but it will also increase the chance of dropouts or non-compliance. Dropouts and non-compliance could be adjusted for by only conducting the study for one year but may drastically reduce the ability to reject the null hypothesis. In addition, as discussed above, there could be casual interference based on the confounding variables of different treatments for each participant based on their oncologist's prescriptions.

Another possible problem is that a double-blind random study may be inefficient at studying rare outcomes. Since statistics on metastatic breast cancer are hard to find due to geography, the sample size may need to be large, which would affect both time and expense even more.

Finally, a problem with this study may be recruiting enough participants. A pilot study may be needed to determine whether those willing to take herbal products and participate in a study will negatively affect randomization and sample size.

### **Summary**

Astragalus due to its chemical constituents of polysaccharides, saponins, and flavonoids demonstrates powerful anti-cancer properties and needs to be explored further in metastatic breast cancer patients to determine the efficacy of this herb in reducing patient mortality and slowing the spread and growth of cancer. A randomized, double-blind prospective cohort trial is proposed for women aged 45-65 who have been recently diagnosed with stage 4 metastatic breast cancer to determine if Astragalus can be used effectively in addition to their current treatment. If found significantly effective,

Astragalus is an immune and cellular metabolic modulating adaptogen with a long-standing history in herbal medicine that could make a safe supplement to invasive breast cancer treatment for better outcomes. In addition, further study could include the effects of Astragalus in non-metastatic breast cancer (stage 1-3) to reduce recurrence rates. Further research is needed in the study of non-toxic herbal remedies as a favorable addition to current breast cancer treatments.

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