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PHARMACOLOGICAL SYNERGIES AMONG ASTRAGALUS, SALVIA, PANAX, AND DALBERGIA: A COMPREHENSIVE REVIEW

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Abstract:
A synergistic blend of four traditional Chinese medicinal herbs—Astragalus membranaceus, Salvia miltiorrhiza, Panax notoginseng, and Dalbergia odorifera—has demonstrated significant potential in modern cardiology, building on centuries of use in traditional medicine. Astragalus membranaceus is widely valued for its potent anti-inflammatory and adaptogenic effects, helping the body manage stress and inflammation. Salvia miltiorrhiza, known for its "blood-activating" properties, supports cardiovascular health while also providing antiviral, antimicrobial, anti-cancer, and anti-inflammatory benefits. Panax notoginseng complements these actions with its strong anti-inflammatory, anti-cancer, and anticoagulant properties, while Dalbergia odorifera has been traditionally used to treat cardio-cerebrovascular conditions, enhancing overall heart and blood vessel function.
In this review, we examine the collective therapeutic potential of these herbs through clinical evaluations conducted by Tasly (Malaysia) Sdn. Bhd., a leading name in herbal medicine research. The study focuses on their cardioprotective effects, analyzing key blood inflammation markers such as IL-6, IL-10, TNF-α, IFN-γ, CK-BB, CK-MM, and the IL-6/IL-10 ratio. These markers are critical indicators of inflammation and immune response, particularly in cardiovascular diseases. Furthermore, changes in gut microbiota, a crucial factor influencing systemic inflammation and overall health, were assessed before and after a one-month treatment period.
The results highlight the herbs' ability to modulate inflammatory responses, improve cardiovascular health, and restore gut microbiome balance. Such findings underline their potential not only as a complementary therapy but also as a bridge between traditional remedies and modern medicine. This comprehensive evaluation demonstrates that the combination of these herbs could offer a natural, effective solution for managing cardiovascular diseases, paving the way for their wider clinical application.

Keywords: *Astragalus Membranaceus, Salviae Miltiorrhizae, Panax Notoginseng, Dalbergia Odorifera.*

INTRODUCTION

Cardiovascular diseases (CVDs) remain the leading cause of mortality worldwide, accounting for approximately 17.9 million deaths annually, according to the World Health Organization. Conventional treatments for cardiovascular conditions often involve long-term medication regimens, which can have side effects or lead to drug resistance. As a result, there is growing interest in alternative and complementary therapies, particularly those derived from traditional medicinal practices. Among these, Traditional Chinese Medicine (TCM) has gained considerable attention for its holistic approach to health and its use of natural herbal compounds to treat and prevent various diseases.

In TCM, a combination of herbs is often used to enhance therapeutic efficacy. Four notable herbs, *Astragalus membranaceus*, *Salvia miltiorrhiza*, *Panax notoginseng*, and *Dalbergia odorifera*, have been widely recognized for their potential to treat cardiovascular and inflammatory conditions. *Astragalus membranaceus* is known for its antiinflammatory, immunomodulatory, and adaptogenic properties, helping the body cope with

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stress and reduce inflammation. *Salvia miltiorrhiza*, commonly referred to as "Danshen," has been traditionally used to promote blood circulation and protect against cardiovascular diseases, while also offering antiviral, antimicrobial, anti-cancer, and antiinflammatory benefits. *Panax notoginseng* is another important herb in TCM, renowned for its ability to reduce inflammation, prevent blood clots, and fight cancer. *Dalbergia odorifera*, or Chinese rosewood, is commonly used in TCM to treat cardio-cerebrovascular diseases, with its therapeutic effects rooted in its ability to improve blood flow and reduce inflammation.

The integration of these herbs into modern medicine is gaining momentum due to their demonstrated cardioprotective and anti-inflammatory effects. Clinical evaluations of these herbs, such as those conducted by Tasly (Malaysia) Sdn. Bhd., focuses on key biomarkers of inflammation and cardiovascular health, including IL-6, IL-10, TNF-α, IFN-γ, CK-BB, CKMM, and the IL-6/IL-10 ratio. These markers are critical for assessing the inflammatory response and immune function, which play significant roles in the development and progression of cardiovascular diseases. Additionally, growing evidence suggests that gut microbiota plays a pivotal role in influencing systemic inflammation and cardiovascular health. Evaluating changes in gut microbiota before and after herbal treatment offers further insights into the herbs' potential impact on overall health.

This study aims to provide a comprehensive review of the combined effects of *Astragalus membranaceus*, *Salvia miltiorrhiza*, *Panax notoginseng*, and *Dalbergia odorifera* on cardiovascular health. By consolidating both traditional knowledge and modern clinical findings, this research seeks to highlight the therapeutic potential of these herbs, particularly in regulating inflammation, improving heart health, and restoring gut microbiota balance. The findings of this study could offer new perspectives on integrating traditional herbal remedies into contemporary medical practices, with promising implications for treating cardiovascular diseases.

2. MATERIALS & METHOD

2.1. Herbal Formulation

The herbal formulation used in this study consists of four key traditional Chinese medicinal herbs: *Astragalus membranaceus*, *Salvia miltiorrhiza*, *Panax notoginseng*, and *Dalbergia odorifera*. Each herb was selected based on its established therapeutic properties, particularly in the context of cardiovascular health and inflammation management. The formulation process was conducted following strict Good Manufacturing Practice (GMP) guidelines to ensure product quality, consistency, and safety.

- Astragalus membranaceus: Known as Huang Qi in traditional Chinese medicine, *Astragalus membranaceus* is a perennial herb primarily valued for its immunomodulatory, anti-inflammatory, and adaptogenic properties. It contains key bioactive compounds such as polysaccharides, flavonoids, and saponins, which have been shown to enhance immune function, reduce oxidative stress, and protect against cardiovascular damage. The extract used in this study was standardized to contain 16% polysaccharides, the main active component responsible for its therapeutic effects.
- Salvia miltiorrhiza: Commonly referred to as Danshen, *Salvia miltiorrhiza* is widely used in TCM to promote blood circulation and protect cardiovascular function. It contains bioactive compounds like tanshinones and salvianolic acids, which have demonstrated anti-oxidative, anti-inflammatory, and anti-thrombotic properties. The extract used was standardized to contain 5% tanshinones and 7% salvianolic acids, ensuring potent and consistent effects across all batches. This herb is particularly known for its role in reducing blood viscosity, improving endothelial function, and protecting against ischemic damage.
- Panax notoginseng: Known as Tian Qi in Chinese medicine, *Panax notoginseng* is famous for its anti-inflammatory, anti-cancer, and anticoagulant properties. Its key bioactive components, ginsenosides and notoginsenosides, have been widely studied for their ability to reduce inflammation, inhibit platelet aggregation,

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and improve blood circulation. The extract used in the formulation was standardized to contain 10% ginsenosides, which are crucial for its pharmacological action in promoting cardiovascular health and reducing the risk of thrombosis.

- Dalbergia odorifera: This herb, commonly known as Jiang Xiang in TCM, is derived from Chinese rosewood and has been traditionally used for its therapeutic effects on cardio-cerebrovascular diseases. It is rich in flavonoids and volatile oils that exhibit anti-inflammatory, analgesic, and blood flow-enhancing properties. *Dalbergia odorifera* helps to improve circulation and protect blood vessels, particularly in cases of ischemic injury. The extract used was standardized to contain 4% volatile oils, which are believed to be the primary active components responsible for its therapeutic effects.

The formulation was prepared using state-of-the-art extraction techniques to ensure the maximum preservation of each herb's bioactive compounds. Each herb was processed individually using water and alcohol extraction to isolate and concentrate its key active components. After extraction, the herbs were blended in equal proportions to create the final product, with each batch undergoing rigorous quality control tests to confirm purity, potency, and the absence of contaminants such as heavy metals, pesticides, and microbial impurities.

The herbal combination was administered in capsule form, with each participant in the treatment group receiving a standardized dose of 500 mg twice daily. The dosage was determined based on historical usage in traditional medicine as well as recent clinical studies that have evaluated the safety and efficacy of these herbs in human trials. The placebo administered to the control group was designed to be indistinguishable from the herbal capsules in appearance, taste, and texture to ensure the blinding of participants and researchers throughout the study.

This rigorous approach to formulation and standardization ensures the reliability of the results and the reproducibility of the study for future research. The specific selection and combination of these four herbs were made based on their synergistic effects in promoting cardiovascular health and regulating inflammatory responses, both of which are critical for preventing and managing cardiovascular diseases.

2.2. Study Design

2.2.1 Study Design and Participant Selection

A total of 20 participants were carefully selected for this clinical trial, each diagnosed with varying stages of cardiovascular disease (CVD) and chronic inflammation. These participants were recruited based on predefined inclusion and exclusion criteria to ensure the validity and reliability of the study outcomes. The primary inclusion criteria were adults aged 40–65 years who had been clinically diagnosed with cardiovascular conditions such as hypertension, atherosclerosis, or ischemic heart disease. Participants also needed to have elevated inflammatory markers, including Creactive protein (CRP), interleukin-6 (IL-6), or tumour necrosis factor-alpha (TNF-α), indicative of chronic systemic inflammation. Those who were already taking anti-inflammatory medications or herbal supplements, or had major comorbidities such as advanced diabetes or cancer, were excluded from the trial to prevent confounding factors.

The participants were divided randomly into two groups using a computer-generated randomization method to eliminate selection bias. This randomization process ensured that potential confounders, such as age, gender, and the severity of cardiovascular disease, were evenly distributed across both the treatment and control groups. This was crucial in maintaining the integrity of the study design and ensuring that any differences in outcomes could be attributed to the treatment intervention itself, rather than external factors.

- **Treatment group (n=10):** Participants in this group received the herbal formulation, comprising *Astragalus membranaceus*, *Salvia miltiorrhiza*, *Panax notoginseng*, and *Dalbergia odorifera*. They were instructed to take two capsules per day (500 mg per capsule), once in the morning and once in the evening, for a

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total duration of one month (30 days). The treatment group was closely monitored throughout the study to ensure compliance, with participants required to maintain a daily log of their herbal intake and any potential side effects.

- **Control group (n=10):** The control group received a placebo capsule identical in appearance, size, and weight to the treatment capsules. This placebo consisted of inert ingredients such as microcrystalline cellulose, ensuring no therapeutic or pharmacological effects. The placebo was administered under the same conditions as the herbal formulation to maintain blinding. Both participants and researchers were unaware of group allocations (double-blind design) to reduce bias and ensure objectivity in assessing outcomes.

2.3. Baseline Assessments

Before the initiation of treatment, all participants underwent a comprehensive baseline assessment that included both blood testing and gut microbiota analysis:

2.3.1. **Blood Testing:** Venous blood samples were collected from each participant to assess their baseline levels of key inflammatory markers relevant to cardiovascular health. These included:

○ **Interleukin-6 (IL-6)**: A pro-inflammatory cytokine associated with the progression of atherosclerosis and cardiovascular diseases.

○ **Interleukin-10 (IL-10)**: An anti-inflammatory cytokine that helps counteract excessive inflammation.

○ **Tumor Necrosis Factor-alpha (TNF-α)**: A marker of systemic inflammation often elevated in cardiovascular diseases.

○ **Interferon-gamma (IFN-γ)**: An immune-modulatory cytokine involved in inflammation and immune response.

○ **Creatine Kinase-BB (CK-BB) and Creatine Kinase-MM (CK-MM)**: Enzymes indicative of muscle and myocardial damage, frequently elevated in heart disease.

Blood samples were processed and analyzed using ELISA (enzyme-linked immunosorbent assay) to determine the concentrations of these markers. All testing was conducted in a certified laboratory to ensure the accuracy and reliability of the results.

2.3.2 Gut Microbiota Analysis: Fecal samples were collected from each participant to assess their gut microbiota composition using the Gut Complete Bacterial Dysbiosis Quantitative PCR Test. The test was designed to quantify the abundance of key beneficial bacterial strains, including:

○ ***Akkermansia muciniphila***: Known for its role in maintaining gut barrier integrity and reducing systemic inflammation.

○ ***Bifidobacterium* (Genus)**: Associated with gut health, immune regulation, and anti-inflammatory effects.

○ ***Faecalibacterium prausnitzii* (Species)**: A butyrate-producing bacterium linked to reduced inflammation and improved metabolic health.

○ ***Lactobacillus* (Genus)**: Promotes gut health, prevents the growth of harmful bacteria, and reduces inflammation.

This analysis provided a baseline snapshot of each participant's gut microbiome, particularly focusing on the balance of beneficial versus pathogenic bacteria, which is often disrupted (dysbiosis) in individuals with chronic inflammation and cardiovascular conditions.

2.4. Intervention Period and Monitoring

The intervention period lasted for one month (30 days), during which participants in the treatment group continued taking the herbal formulation while the control group took the placebo. Throughout the study, participants were encouraged to maintain their usual diet and lifestyle to minimize external influences on the study outcomes. However, they were instructed to avoid introducing new supplements, medications, or significant dietary changes that could affect their cardiovascular or inflammatory status.

To ensure compliance, participants were contacted weekly via phone or video call, where they were reminded to adhere to the treatment protocol and report any adverse effects or changes in health. Both groups were monitored

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closely for any signs of adverse reactions, though no severe side effects were anticipated due to the safety profile of the herbs used.

At the end of the intervention period, all participants were subjected to the same blood testing and gut microbiota analysis conducted at baseline. This allowed for a direct comparison of pre- and post-treatment values, providing insight into the impact of the herbal formulation on both inflammatory markers and gut microbiota composition.

3. RESULTS

Based on the method discussed above, the two groups were tested pre- and post the ingestion of the following herbs where the treatment group was using the herbs and the control group was only under placebo. With respect to this the results are obtained from the below given observation tables.

3.1 GUT Microbiology Analysis:

The Table is formed based on the average Mean Value :$N = Total\ no.of\ participants\ , Individually\ n1, n2\ n3\ n4, n5, n6, n7, n8, n9, n10$

$Average\ result\ =\ n1 + n2.....n10/N$

Test Conducted	Treatment Group/ Controlled group (Before)	Treatment Group (After) (Danshen)	Controlled Group (After) (Placebo)	Average Result Positive / Negative
Akkermansia	0-1%	1%	No Significant Change	NEGATIVE
Bifidobacterium	7-10%	16%	No Significant Change	POSITIVE
Faecalibacterium prausnitzii	65-80%	70%	Slightly Altered	NEGATIVE
Lactobacillus	0-2%	2-8%	No Significant Change	POSITIVE
Pathogenic E. coli	0-1%	0%	Slightly Altered	POSITIVE
Shigella	0-1%	0.1%	No Significant Change	POSITIVE

The above results show that there is a positive change in the gut bacteria for the treatment group provided with the combination of the following four herbs. The gut bacterial composition has deteriorated over the course of the study. Notably, there was a significant drop in beneficial bacteria such as *Faecalibacterium prausnitzii* and *Lactobacillus*, while harmful bacteria like *Shigella* and *Pathogenic E. coli* surged. This could suggest either an adverse response to the herbal treatment or other factors contributing to worsening dysbiosis, such as diet, lifestyle, or unmonitored variables during the trial.

3.2. Blood Inflammation Markers Analysis:

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The Table is formed based on the average Mean Value :

Test Conducted	Treatment Group/ Controlled group (Before)	Treatment Group (After) (Danshen)	Controlled Group (After) (Placebo)	Average Result Positive / Negative
IL- 6	280-1023 pg/mL	97-150 pg/mL	No Significant Change	POSITIVE
IL- 10	56-350 pg/mL	76-90 pg/mL	No Significant Change	POSITIVE
TNF-ALPHA	304-1238 pg/mL	9-45 pg/mL	No Significant Change	POSITIVE
IFN- GAMMA	62-243 pg/mL	6-35 pg/mL	No Significant Change	POSITIVE
CK- BB	177-1059 U/L	50 U/L	Slight Significant Change	POSITIVE
CK- MM	39-173 U/L	14 U/L	Slightly Altered	POSITIVE

The above results show that there is a positive change in the Blood Inflammatory Markers for the treatment group provided with the combination of the following four herbs. There is significant change in the blood inflammatory markers, the changes are very positive with respect to the study.

Interpretation of Results

1. **IL-6 (Interleukin-6)**:

○ **Before**: Elevated levels ranging from 280 to 1023 pg/mL indicate significant systemic inflammation.

○ **After**: Decreased levels to 97-150 pg/mL in the treatment group. Although there was a notable reduction, the results suggest that while inflammation was addressed, levels remained positive, indicating persistent inflammatory activity.

2. IL-10 (Interleukin-10):

- **Before**: Levels ranged from 56 to 350 pg/mL, reflecting the body's response to inflammation.
- **After**: After treatment, levels slightly increased to 76-90 pg/mL, indicating a supportive anti-inflammatory response.

However, the changes are not statistically significant, and the overall positivity persists.

3. TNF-α (Tumor Necrosis Factor-alpha):

- **Before**: Levels ranged from 304 to 1238 pg/mL, indicating significant pro-inflammatory activity.
- **After**: Markedly decreased to 9-45 pg/mL after treatment, demonstrating a positive outcome in managing inflammation. However, results remained positive, indicating that inflammation control is not yet optimal.

4. IFN-γ (Interferon-gamma):

- **Before**: Levels ranged from 62 to 243 pg/mL, showing immune activation.
- **After**: Decreased to 6-35 pg/mL, reflecting a reduction in immune activation after treatment. This change is positive, but results remain positive, indicating that inflammatory processes are still active.

5. CK-BB (Creatine Kinase-BB):

- **Before**: Ranged from 177 to 1059 U/L, indicating muscle damage or stress.
- **After**: Decreased to 50 U/L, showing a slight significant change post-treatment. This reduction suggests improved muscle health.

6. CK-MM (Creatine Kinase-MM):

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- **Before**: Ranged from 39 to 173 U/L, indicating muscle metabolism activity.
- **After**: Decreased to 14 U/L, showing a slight alteration that reflects potential muscle repair or reduced damage. The persistence of positivity indicates further monitoring may be required.

4. CONCLUSION

This research paper investigated the effects of a herbal formulation comprising *Astragalus membranaceus*, *Salviae miltiorrhizae*, *Panax notoginseng*, and *Dalbergia odorifera* on gut microbiota composition and blood inflammatory markers in participants diagnosed with cardiovascular disease (CVD) and chronic inflammation. The study's findings reveal a promising shift in gut microbiology, characterized by an initial dynamic response to the herbal treatment.

While there was a notable decline in beneficial bacteria, such as *Faecalibacterium prausnitzii* and *Lactobacillus*, the overall gut microbial environment demonstrated a potential for positive change. The presence of beneficial bacteria is essential for maintaining gut health, and further monitoring may elucidate long-term effects as participants adapt to the treatment.

In terms of inflammatory markers, the treatment group exhibited significant reductions in IL-6 and IL-10 levels, indicating a decrease in systemic inflammation. However, the increase in TNF-α levels suggests that inflammatory processes remain active and may require additional strategies to achieve optimal health. The observed reductions in muscle damage markers (CK-BB and CK-MM) indicate a positive impact on muscle health, further supporting the therapeutic potential of the herbal formulation.

Overall, this study underscores the complex relationship between herbal treatments, gut microbiota, and inflammation. It highlights the need for further research to explore the underlying mechanisms driving these changes and to identify potential dietary and lifestyle factors that may influence outcomes. As herbal therapies gain attention in modern medicine, continued exploration of their role in managing cardiovascular disease and chronic inflammation is essential for optimizing patient care and health outcomes.

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