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# *The Pharmacological Effects and Clinical Application of the Combination of Traditional Chinese Medicine Compound and Western Medicine in Acute Myelogenous Leukemia*

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***Abstract.*** Acute myelogenous leukemia is a serious malignant hematological disorder that significantly endangers human health. Currently, its treatment still faces challenges such as chemotherapy resistance, significant toxic side effects, and high recurrence rate. In recent years, the combination of traditional Chinese and Western medicine has gradually become a prominent research focus in the clinical study of acute myelogenous leukemia. Although Western medical treatments such as chemotherapy and targeted therapy have continuously improved, how to enhance efficacy and reduce toxic side effects remains a key issue that urgently needs to be addressed. Due to its multi-component and multi-targeting characteristics, traditional Chinese medicine demonstrates unique advantages in the treatment of leukemia. This review aims to summarize the pharmacological effects and unique advantages of traditional Chinese medicine compound prescriptions in the treatment of acute myelogenous leukemia. Taking three TCM compound prescriptions—Zhebei Huangqin Decoction, Dingqing Tablets, and Yiqi Yangyin Formula—as examples, this article systematically reviews the clinical progress of integrating traditional Chinese and Western medicine in acute myelogenous leukemia, with the aim of providing a reference for further research and new drug development in TCM-based anti-leukemia therapy.

***Keywords:*** Acute myelogenous leukemia, Traditional Chinese medicine, Compound, Mechanism of action, clinical application

## 1. Introduction

Acute myelogenous leukemia (AML) is a malignant disease of the hematological system that originates in the bone marrow. It is a common type of leukemia and its incidence significantly increases with age. Genetic mutations are the fundamental cause of its pathogenesis [1]. Although modern medicine has adopted traditional methods such as chemotherapy, hematopoietic stem cell transplantation, and supplementary blood transfusion therapy in the treatment of leukemia, and has further developed new methods such as targeted therapy, immunotherapy, and small molecule drug treatment, there are still problems such as poor efficacy and the possibility of patients developing drug resistance. In this context, traditional Chinese medicine treatment for acute myelogenous leukemia has certain characteristics and advantages. A large number of studies have confirmed that

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traditional Chinese medicine treatment for acute leukemia has good efficacy. Combined with Western chemotherapy, it can enhance the sensitivity of chemotherapy drugs, improve the chemotherapy effect, alleviate bone marrow suppression, and reduce toxic side effects, etc. [2]. Therefore, this article aims to review and summarize the clinical efficacy of the combination of traditional Chinese medicine formulas and Western medicine in the field of acute myelogenous leukemia in the past five years, in order to provide more ideas and basis for subsequent research in this field. This article will systematically review the treatment mechanism of Western medicine, the pharmacology and clinical research of three traditional Chinese medicine formulas, as well as the synergistic advantages of integrating traditional and Western medicine.

## 2. Application of western medicine in leukemia treatment and its mechanism of action

### 2.1. The mechanism of action and clinical application of cytarabine arabinoside

Cytosine arabinoside (Ara-C) is a type of pyrimidine-based antimetabolite drug and is one of the most commonly used drugs for treating leukemia. After being converted into the active form of arabinoside triphosphate (Ara-CTP) through three steps in the body, Ara-C can be incorporated into the nucleotide chains of deoxyribonucleic acid (DNA), inhibiting DNA synthesis by preventing chain elongation, causing chain breaks, and affecting chain replication. As a S-phase-specific drug, it can inhibit the proliferation of tumor cells and exert anti-tumor effects. Moreover, Ara-C induces apoptosis in HL-60 cells and leads to the downregulation of c-Myc and B-cell lymphoma-2 (BCL-2) genes [3,4]. In clinical practice, different doses of Ara-C show different therapeutic effects and adverse reactions. High-dose consolidation treatment can better control the condition, but the adverse reactions are more severe; while medium and low doses have a higher risk of recurrence and are difficult to balance efficacy and safety [5].

### 2.2. The mechanism of action and clinical applications of daunorubicin

Daunorubicin (DNR), an anthracycline drug, can penetrate into deoxyribonucleic acid (DNA) and inhibit the synthesis of DNA and ribonucleic acid (RNA). It has now been used in the induction and remission treatment of AML [6]. After administration of DNR, it can undergo liver metabolism to form daunorubicin alcohol, which has anti-tumor activity and can penetrate into DNA to affect the synthesis of DNA and RNA. At the same time, it selectively acts on purine nucleosides, helping to control the condition of AML [6]. According to research, the clinical effective rate of combining DNR with Ara-C is higher than that of using Ara-C alone, and it can also reduce the impact on immune function. At the same time, DNR + Ara-C can inhibit the growth and reproduction of tumor cells, reduce the release of various inflammatory cytokines, and thus can down-regulate the expression of VEGF, bFGF, sVCAM-1, and sICAM-1 [6].

### 2.3. Mechanism of action and clinical application of idarubicin

Idarubicin (IDA) is a derivative of the anthracycline drug DNR. Compared with DNR, it has higher affinity and liposolubility, and is more capable of penetrating the cell membrane, exerting the effects of inhibiting nucleic acid synthesis, promoting DNA lysis and cell apoptosis. It also has low drug resistance and fewer adverse reactions [7]. Studies have shown that the treatment regimen of IDA combined with Ara-C is more suitable for the induction and remission treatment of AML patients than the combination of DNR and Ara-C, and it prolongs the median survival time of AML patients and reduces the disease recurrence rate. However, there is no significant difference between the two

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regimens in terms of adverse reactions, including gastrointestinal reactions, skin and mucosal bleeding, and cardiotoxicity [8].

## 3. The application forms of traditional chinese medicine compound prescriptions in the treatment of acute myelogenous leukemia

This text will systematically review the Zhebei Huangqin Decoction, Dingqing Tablets, and Yi Qi Yangyin Formula from three aspects: the characteristics of the formula, the mechanism of pharmacological action, and clinical application.

### 3.1. Zhebei Huangqin Decoction

The basic formula of Zhebei Huangqin Decoction consists of Scutellaria baicalensis, Qingdai, Zhebeimu, Huoxiaoren, Chuanxiong, Hanfangzi, Maiweng, Gancao. The prescription may be adjusted according to the specific condition and symptoms. Among them, Zhebeimu clears heat and detoxifies, reduces phlegm and relieves cough, while Chuanxiong and Hanfangzi promote blood circulation and relax the meridians. When combined with the bitter and cold Scutellaria baicalensis and Qingdai, they eliminate dampness and heat, as well as detoxify and eliminate toxins.

According to research, when this prescription is used in combination with Western medicine, it can alleviate chemotherapy-induced bone marrow suppression. The objective response rate is much higher than that of the group using Western medicine alone. At the same time, it can also reduce the risk of infection. The immune indicators CD3+, CD4+, and CD8+ are also significantly higher than those of the group using Western medicine alone. It can effectively improve immune function and has high safety.

The main reasons are as follows: In the Zhebei Huangqin Decoction, Scutellaria baicalensis and indigo naturalis enhance the sensitivity of tumor cells to chemotherapy drugs and reverse tumor multidrug resistance. At the same time, their blood-activating and blood-stasis-resolving effects improve blood circulation in the bone marrow, promote normal hematopoietic function, and enhance the body's anti-tumor immune response. In addition, components such as baicalin and hamiphenanthrene can regulate immune factors and improve the efficiency of immune signal transmission. The ingredients like madong and licorice in the formula can protect the hematopoietic microenvironment of the bone marrow and accelerate the regeneration and functional recovery of immune cells. Chuanxiong can inhibit the release of pro-inflammatory mediators, block the COX-2 related signaling pathway, and reduce the invasiveness of leukemia. Beimu zhen can interfere with tumor angiogenesis and inhibit the formation of new blood vessels in the bone marrow; indigo naturalis, lotus seed, and others can selectively inhibit the proliferation of leukemia primitive cells and exert anti-tumor effects [9]. Moreover, DNR belongs to a non-specific anti-tumor drug, and Ara-C is a cell cycle-specific drug. Both can inhibit DNA synthesis and interfere with the proliferation of tumor cells. However, the commonly used DA regimen (DNR+Ara-C) may lead to the upregulation of WIP1 mRNA of oncogenes and the downregulation of P53 mRNA of tumor suppressor genes. Among them, WIP1 is a well-known oncogene, while P53 is a classic tumor suppressor gene. Studies have shown that the Zhebei Huangqin Decoction can downregulate the expression of WIP1 mRNA of oncogenes and upregulate the expression of P53 mRNA of tumor suppressor genes, which can restore the activity of P53 and activate the P53 pathway, thereby significantly inhibiting the proliferation of leukemia cells. This indicates that the Zhebei Huangqin Decoction has certain reparative and regulatory effects: it can re-activate the P53 tumor suppressor pathway, partially

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reverse chemotherapy resistance, and, when used in combination with chemotherapy drugs, enhance the overall anti-tumor efficacy [10].

### 3.2. Qingting tablets

Dingqing Tablets are an effective treatment for acute myeloid leukemia. They are composed of twelve traditional Chinese medicines including realgar, Scutellaria baicalensis, artificial rhinoceros horn, Gardenia jasminoides, PericarpiumCitri Reticulatae, and Benzoin. Among them, realgar can detoxify, fight cancer, dry dampness and eliminate phlegm; Qingdai and Gardenia are used together to achieve the effects of clearing heat, detoxifying, reducing fire and cooling blood; Pericarpium Citri Reticulatae can invigorate qi, strengthen the spleen, eliminate phlegm and dry dampness. When Pericarpium Citri Reticulatae is combined with Gardenia, it can enhance the dampness-eliminating effect of realgar and also harmonize the cold and hot properties in the formula.When all these herbs are used together, they achieve good therapeutic effects and can be used for the treatment of acute myelogenous leukemia.

Studies have shown that in the group treated with Dingqing Tablets combined with Western medicine, patients' symptoms such as fever, skin or mucosal bleeding, fatigue, dry mouth and throat, etc. have significantly improved, and the total effective rate is higher than that of the group using Western medicine alone.Comparing the levels of bone marrow blast cells in the two groups, the group using the combined drugs has significantly lower levels than the group using Western medicine alone, suggesting that it has more sufficient inhibition of leukemia cells and a better disease control effect. After treatment, the levels of serum LDH and $\beta_2$-MG in both groups decreased compared to before treatment, and the reduction in the combined treatment group was significantly better than that of the control group. In terms of safety, the incidence of adverse reactions in the group using combined Chinese and Western medicine was also lower [11].

Dingqing Tablets exert anti-leukemia effects through multi-component, multi-target and multi-pathway synergy: Network pharmacology analysis has screened out its core active ingredients (such as kaempferol, quercetin, naringenin, etc.), mainly acting on key targets such as TP53, AKT1, MMP9, CASP3, and TNF. On the one hand, by up-regulating the tumor suppressor gene TP53 and activating the CASP3 pathway, it promotes leukemia cell apoptosis and inhibits abnormal cell proliferation; on the other hand, it regulates the AKT1 pathway, reverses chemotherapy resistance, and inhibits MMP9 to reduce tumor angiogenesis and invasion. On the other hand, it regulates the AKT1 pathway, reverses chemotherapy resistance, and inhibits MMP9 to reduce tumor angiogenesis and invasion. At the same time, it inhibits inflammatory signaling pathways such as TNF and IL-17, reduces the risk of infection, and ultimately achieves the effect of inhibiting leukemia progression and enhancing chemotherapy sensitivity [12].

### 3.3. Tonifying Qi and Nourishing Yin Formula

The Qi-Boosting and Yin-Nourishing Formula is composed ofradix pseudostellariae, Huangqi, Shengdihuang, Baihuashtelacca, Banxiaohui, Mai Dong, Bai Zhi, Fu Ling, Mudanpi, Huangjing, Nüzhenzi, and Gancao. Clinically, it can be adjusted according to the specific condition and physical constitution of the patient. The formula consists of Radix Pseudostellariae, which nourishes the spleen and lungs and replenishes qi and generates fluids; Huangqi, which replenishes qi, raises yang, and strengthens the exterior; together, they serve as the main ingredients, laying the foundation for nourishing qi and reinforcing the body. Peony bark and Shengdihuang clear heat and nourish yin, activate blood and cool blood; Baihuashtelacca and Banxiaohui clear heat, detoxify, and reduce

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swelling and disperse nodules. Together, they achieve the effects of clearing heat, cooling blood, and detoxifying and fighting cancer. Mai Dong andradix pseudostellariae are combined to enhance the ability to nourish yin, moisten the lungs, and generate fluids; Bai Zhi replenishes qi and generates blood, and when used with Fu Ling, it can tonify the spleen, dry dampness, and protect the spleen. Huangjing nourishes qi and nourishes yin, assisting in moistening the lungs; Nüzhenzi nourishes the liver and kidneys; Gancao harmonizes all the herbs, enabling the entire formula to achieve the effects of nourishing qi and yin, clearing heat and detoxifying, tonifying the spleen and benefiting the kidneys.

Compared with treatment with Western medicine alone, the combination of the tonifying qi and nourishing yin formula with Western medicine can better protect patients' immune function: it can maintain the levels of $CD3^+$ and NK cells, increase the levels of $CD4^+$ and the ratio of $CD4^+/CD8^+$, and enhance the anti-tumor immune surveillance and immune regulation ability. At the same time, it can significantly reduce the proportions of white blood cells and bone marrow blast cells, alleviate the burden of leukemia; improve the trend of platelet and hemoglobin first decreasing and then increasing, and promote the recovery of hematopoietic function. In addition, it can more effectively lower the VEGF level to inhibit tumor angiogenesis, improve the clinical objective response rate (ORR), and it does not increase adverse events [13].

The aqueous extract of Astragalus in the formula can stimulate the proliferation and differentiation of erythroid progenitor cells, promote the transition of erythroid cells in the $G_0$ phase to the S phase, improve the morphology of the bone marrow cavity, and exert a hematopoietic protective effect by increasing WBC, Hb, and PLT levels; at the same time, it can enhance the phagocytic function of T cells and dendritic cells, improve the body's immunity, and promote the apoptosis of tumor cells. The ethanol extract of Rehmannia glutinosa can shorten the bleeding and clotting time, optimize blood routine indicators, and coordinate the regulation of immunity and hematopoiesis. Poria cocos, moutan root bark, Atractylodes, and Glycyrrhiza can promote the proliferation of T cells, enhance the killing activity of macrophages and NK cells against AML cells, inhibit the proliferation of tumor cells, and promote the reproduction of bone marrow hematopoietic progenitor cells. Trichosanthes kirilowii can improve immune function and protect the hematopoietic system; Sophora flavescens has a mild inhibitory effect on AML cells; Atractylodes and Palustris have the functions of protecting bone marrow cells, increasing white blood cell counts, and inducing apoptosis of leukemia cells [13,14].

## 4. Conclusion

In traditional Chinese medicine theory, acute myelogenous leukemia (AML) can be classified under the category of "bone marrow toxicity". The core pathogenesis of AML is qi and yin deficiency and internal accumulation of pathogenic toxins. Although chemotherapy drugs can kill leukemia cells, they consume the patient's qi and yin, aggravate the internal accumulation of pathogenic toxins, and subsequently damage the bone marrow , triggering bone marrow suppression. The Chinese herbal formulas listed in this article, such as the Qi-strengthening and Yin-nourishing formula, Dingqing tablet, and Zhebei Huangqin decoction, all follow the basic treatment principle of "strengthening the body and eliminating the pathogen". Through qi-strengthening and yin-nourishing drugs to assist in strengthening the body and protecting the bone marrow and immune function, and using heat-clearing and toxin-resolving drugs to inhibit the proliferation of leukemia cells, they can cooperate with chemotherapy to exert synergistic effects, reduce toxicity, improve bone marrow suppression and immune status. Western chemotherapy (such as Ara-C, daunorubicin [DNR], etc.) can effectively inhibit the proliferation of tumor cells, but it has limitations including bone marrow

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suppression and drug resistance; while Chinese herbal formulas can show significant advantages in enhancing chemotherapy sensitivity, reversing chemotherapy resistance, reducing bone marrow suppression, improving immune function and regulating the tumor microenvironment through multi-component, multi-target and multi-pathway synergistic effects. Combined use can improve the clinical remission rate without increasing adverse reactions, and has important clinical promotion value. However, current research still faces challenges such as complex components of Chinese herbal formulas, unclear pharmacological basis of efficacy, and low bioavailability of active ingredients. In the future, emerging technologies such as systems biology and network pharmacology should be used to deeply explain their multi-target action mechanisms, and new drug delivery systems should be actively developed to promote the broader application of Chinese medicine in leukemia treatment. This article only selects three representative Chinese herbal formulas—Zhebei Huangqin Decoction, Dingqing Tablet, and Qi-strengthening and Yin-nourishing Formula—for discussion. It fails to cover all effective prescriptions for the clinical treatment of acute myelogenous leukemia, and the related research and application content is not comprehensive enough. At the same time, the comparison analysis among various prescriptions is relatively brief, and the mechanism exploration is mostly based on existing research summaries, lacking deeper mechanism mining and integrated analysis. In the future, the scope of prescriptions could be expanded, and the comparison and mechanism studies could be improved to make the discussion more systematic and complete.

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