Mechanism Study on Synergistic Regulation of Inflammatory-Metabolic Network in Type 2 Diabetes Mellitus by Multi-Components of Chinese Herbal Compound Formula

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ABSTRACT The progression of type 2 diabetes mellitus is closely interconnected with chronic low-grade inflammation and glycolipid metabolic disorders through complex network interactions. Intervention targeting a single molecular node fails to block the cascade amplification effects of such networks. Chinese herbal compound formulas possess unique advantages in regulating complex pathological networks owing to their integrative characteristics of multiple components and multi-target actions. This paper analyzes the mechanisms by which multiple components of Chinese herbal compound formulas synergistically modulate inflammatory-metabolic networks. An argumentative framework is constructed from three dimensions: the pathological coupling basis, target mapping of compound formulas, and synergistic pathway mechanisms. Combined with animal experiments as well as transcriptomic and metabolomic data, this study identifies the interaction nodes of the AMPK and AKT/mTOR pathways within inflammatory-metabolic networks, and clarifies the bidirectional regulatory effects of multi-component synergistic intervention on insulin resistance and chronic inflammation. The findings provide a theoretical foundation for the clinical application of Chinese herbal compound formulas in the treatment of type 2 diabetes mellitus.

INDEX TERMS Chinese herbal compound formula; type 2 diabetes mellitus; inflammatory-metabolic network; multi-component synergy; network pharmacology

I. INTRODUCTION

Type 2 diabetes mellitus (T2DM) is no longer merely regarded as a disorder characterized by abnormal glycometabolism. Mounting evidence indicates that its essence is a systemic pathological condition intertwined by chronic low-grade inflammation and metabolic disorders. Immune cell infiltration and inflammatory factor secretion occur in metabolic organs including adipose tissue, liver and skeletal muscle under long-term high-glucose and high-lipid conditions, forming a mutually reinforcing network structure with the impairment of insulin signaling pathways, which endows disease progression with complex features of multi-pathway and multi-target coupling. Chemical drugs developed for single targets can effectively reduce blood glucose in the short term, yet they fail to simultaneously intervene in the networked crosstalk between inflammation and metabolism. Many patients still face the risk of progressive chronic complications after long-term medication. Chinese herbal compound formulas have accumulated abundant clinical experience in treating diabetes (Xiaoke disease) over thousands of years [1]. Their integrated mode of action featuring multi-components, multi-targets and multi-pathways is naturally consistent with the complex pathological structure of the inflammatory-metabolic network in T2DM. With the advancement of systematic biology approaches such as network pharmacology, transcriptomics and metabolomics, the interpretation of the action mechanisms of Chinese herbal compound formulas has gradually shifted from vague holistic regulation to concrete component-target-pathway correlations, which provides a feasible route to uncover the molecular basis of multi-component synergistic effects. Existing studies on Chinese herbal compound formulas for T2DM have covered multiple aspects including inflammation suppression, insulin sensitization and intestinal flora regulation. Nevertheless, most researches tend to separately describe the effects of a single pathway or individual component, lacking systematic elaboration on the interactive nodes of inflammation and metabolism from an overall network perspective.

Few studies cross-validate prediction outcomes of network pharmacology with animal experiments and multi-omics data. In view of the above gaps, this paper systematically analyzes the mechanisms through which multi-components of Chinese herbal compound formulas synergistically regulate the inflammatory-metabolic network in T2DM from four progressive dimensions: the coupling basis of pathological networks, target mapping of the material basis of compound formulas, pathway mechanisms of synergistic effects, and multi-omics experimental verification. It aims to clarify the specific pathways by which multi-components act on the inflammatory-metabolic network, and offer references for modern mechanistic research and clinical transformation of Chinese herbal compound formulas..

II. PATHOLOGICAL CORRELATION BASIS OF INFLAMMATORY-METABOLIC NETWORK IN TYPE 2 DIABETES MELLITUS

A. BIDIRECTIONAL CAUSAL RELATIONSHIP BETWEEN GLYCOLIPID METABOLIC DISORDERS AND CHRONIC INFLAMMATORY RESPONSES

The relationship between glycolipid metabolic disorders and chronic inflammatory responses is not a simple sequential causality, but a continuously self-amplifying cycle. Excessive long-term energy intake abnormally enlarges adipocytes and facilitates macrophage infiltration into adipose tissue. The secreted tumor necrosis factor-α (TNF-α) and interleukin-6 (IL-6) enter the circulatory system, impairing the responsiveness of the liver and skeletal muscle to insulin signals, reducing glucose uptake efficiency and boosting triglyceride synthesis. Elevated free fatty acids induced by dyslipidemia further activate macrophages via Toll-like receptor 4 (TLR4), triggering additional secretion of inflammatory cytokines. This creates a self-perpetuating vicious cycle in which metabolic disorders and inflammatory responses reinforce one another.

The liver plays a dual role in this cycle. On one hand, peripheral inflammatory signals stimulate hepatic lipid deposition and insulin resistance; on the other hand, hepatic acute-phase proteins exert feedback effects to exacerbate systemic inflammation, rendering the liver a pivotal organ where metabolic disorders and inflammatory responses converge. As the primary site of glucose uptake, skeletal muscle exhibits impaired mitochondrial oxidative phosphorylation under chronic inflammatory conditions. This leads to intracellular accumulation of lipid metabolites, which disrupt the phosphorylation of insulin receptor substrates (IRS).

The cross-talk between inflammation and metabolism across multiple organs endows the pathological progression of type 2 diabetes mellitus (T2DM) with distinct network characteristics. Single interventions targeting blood glucose or inflammation alone fail to block the cascade amplification of the overall network. This intertwined bidirectional coupling forms the pathological foundation for interpreting the multi-component synergistic effects of Chinese herbal compound formulas.

B. DRIVING EFFECT OF INFLAMMATORY SIGNALING PATHWAYS ON THE DEVELOPMENT OF INSULIN RESISTANCE

The driving effect of inflammatory signaling pathways on insulin resistance mainly manifests in the disruption of downstream receptor signal transduction by inflammatory cytokines. Activated via the nuclear factor κB (NF-κB) pathway, tumor necrosis factor-α (TNF-α) and interleukin-1β (IL-1β) prompt IκB kinase β (IKKβ) to induce aberrant serine phosphorylation of insulin receptor substrate 1 (IRS-1), inhibiting normal tyrosine phosphorylation. This suppresses the signaling efficiency of phosphatidylinositol 3-kinase (PI3K) and protein kinase B (Akt), and hinders the membrane translocation of glucose transporter 4 (GLUT4).

The c-Jun N-terminal kinase (JNK) pathway also exerts a critical regulatory role. Its persistent activation aggravates serine phosphorylation of insulin receptor substrates, resulting in signal transduction defects at the insulin receptor level. Endoplasmic reticulum stress represents another convergence point of inflammatory signals and metabolic disorders. Activation of the unfolded protein response not only upregulates the transcription of inflammatory cytokines but also directly impairs insulin signal transduction, tightening the coupling between inflammation and metabolic dysfunction.

Polarization shifts of adipose tissue macrophages cannot be overlooked either. An elevated proportion of pro-inflammatory M1 macrophages sustains high local concentrations of pro-inflammatory cytokines, suppressing insulin sensitivity in adjacent adipocytes. The above mechanisms demonstrate that inflammatory signaling pathways are not passive byproducts of peripheral metabolic abnormalities, but core factors actively driving insulin resistance. This driving relationship provides clear targets for subsequent multi-component targeted intervention against inflammatory pathways.

C. FUNCTIONAL COUPLING CHARACTERISTICS OF KEY NODES IN THE INFLAMMATORY-METABOLIC NETWORK

The functional coupling characteristics of key nodes in the inflammatory-metabolic network are embodied by a small number of core molecules that simultaneously participate in two originally separate pathway systems: inflammatory regulation and metabolic modulation. As a core cellular energy sensor, decreased AMP-activated protein kinase (AMPK) activity not only triggers disorders in fatty acid oxidation and glycogen synthesis, but also weakens its negative regulatory effect on the nuclear factor κB (NF-κB) pathway, further amplifying inflammatory responses. Therefore, AMPK serves as a canonical node linking metabolic imbalance and inflammatory activation.

The NLRP3 inflammasome represents another critical coupling structure. Its assembly relies on metabolic signals induced by mitochondrial dysfunction and elevated reactive oxygen species (ROS). After assembly, the secreted

interleukin-1β (IL-1β) in turn aggravates insulin resistance, enabling bidirectional transmission between metabolic disorders and inflammatory activation at this node.

Peroxisome proliferator-activated receptor γ (PPARγ) is an essential regulator of adipocyte differentiation and lipid metabolism, and its expression is closely correlated with macrophage polarization. Reduced PPARγ activity drives macrophage polarization from anti-inflammatory M2 phenotype to pro-inflammatory M1 phenotype, thereby translating lipid metabolic abnormalities into altered inflammatory phenotypes.

These nodes usually exhibit high connectivity within the network structure, and changes in their functional status can simultaneously affect multiple downstream pathways. Compared with single peripheral targets in the network, such coupling nodes exert a more prominent impact on overall network homeostasis. Meanwhile, they provide a theoretical anchor for identifying effective multi-components from compound formulas that can regulate both inflammation and metabolism simultaneously [2].

III. CHEMICAL MATERIAL BASIS AND TARGET MAPPING OF MULTI-COMPONENTS IN CHINESE HERBAL COMPOUND FORMULAS

A. EXTRACTION, IDENTIFICATION AND CHARACTERIZATION OF ACTIVE COMPONENT GROUPS IN COMPOUND FORMULAS

Extraction, identification and characterization of active component groups constitute the material basis for subsequent target mapping and mechanistic analysis. Ethanol gradient extraction combined with macroporous resin column separation can proportionally enrich components of different polarities in compound formulas, including flavonoids, alkaloids and polyphenols. Subsequently, ultra-high performance liquid chromatography-tandem mass spectrometry (UPLC-MS/MS) is adopted for separation and identification. Compounds are confirmed by matching retention time, parent ion and fragment ion information with standard databases.

Multiple anti-diabetic compound formulas repeatedly contain berberine from Coptis chinensis, astragaloside IV from Astragalus membranaceus, and filicic acid from Crataegus pinnatifida, indicating that these ingredients may form the core material basis for the holistic efficacy of compound formulas. During component identification, the Lipinski's Rule of Five is applied to preliminarily screen compounds according to their absorption, distribution, metabolism and excretion (ADME) profiles. Components with excessively low bioavailability or poor oral activity are excluded, so that the component dataset incorporated into subsequent network analysis can better reflect actual in vivo exposure.

To intuitively display the correspondence between major active components of compound formulas and their representative targets, the representative identified components and relevant information are summarized in Table 1. Most components listed in Table 1 possess dual pharmacological activities of anti-inflammation and glycolipid metabolism regulation, and several components recur in compound formulas from different origins. This finding suggests that these ingredients are likely the common foundation underlying the synergistic effects of Chinese herbal compound formulas, rather than random combinations unique to a single prescription, and provides screening criteria for the subsequent construction of component-target network models [3].

B. CONSTRUCTION OF INGREDIENT-TARGET-PATHWAY NETWORK MODEL

The construction of the ingredient-target-pathway network model takes the identified active ingredients as the starting point. Target prediction databases are adopted to obtain potential targets of each ingredient, which are then intersected with type 2 diabetes-related disease target databases to acquire the set of shared potential targets between the herbal compound and type 2 diabetes. On this basis, Cytoscape software is used to construct a three-layer network of ingredients, targets and pathways, and topological indicators such as node degree centrality are calculated to identify core nodes with high connectivity within the network. The formula for node degree centrality is as follows:

$$C_D(v) = \frac{k_v}{n-1}$$

Where k_v refers to the number of edges connected to node v, and n stands for the total number of network nodes. A higher value of this indicator means the corresponding target has denser correlations with other ingredients or pathways, and is more likely to be the convergence point for synergistic effects of multiple ingredients.

Pathway enrichment analysis further maps key targets to well-known biological pathway databases to clarify the specific distribution of these targets in inflammatory and metabolic pathways. This network model not only demonstrates the corresponding relationships between ingredients and targets, but also reveals that multiple ingredients may converge on adjacent pathways through different targets, which is the direct manifestation of multi-ingredient synergistic effects at the molecular network level. It provides a structured framework for subsequent analysis of specific synergistic mechanisms [4].

C. MAPPING CHARACTERISTICS BETWEEN COMPOUND TARGETS AND DISEASE NETWORK NODES

The mapping characteristics between compound targets and disease network nodes are reflected in massive overlaps and complementary functional regions between the two types of network structures. Comparing the predicted compound targets with the aforementioned core nodes of the inflammatory-metabolic network, it is found that AMPK, PPARγ, NLRP3 and other core coupling nodes all appear in the intersection set. This proves that the multi-ingredients of the compound do not randomly distribute on the periphery

TABLE 1. Representative active components of compound formulas and their key targets

Category of Ingredients	Representative Ingredients	Source Medicinal Herbs	Key Targets	Main Pharmacological Activities
Alkaloids	Berberine	*Coptis chinensis*	AMPK, IKKβ	Hypoglycemic, anti-inflammatory
Saponins	Astragaloside IV	*Astragalus membranaceus*	AKT, TLR4	Insulin sensitizing, anti-inflammatory
Flavonoids	Quercetin	*Crataegus pinnatifida*	NLRP3, PPARγ	Inhibit inflammasome
Organic acids	Mellitic acid	*Crataegus pinnatifida*	PPARα	Regulate lipid metabolism
Saponins	Ginsenoside Rb1	*Panax ginseng*	PI3K, GSK3β	Improve insulin signaling

of the disease network, but concentrate on hub positions with high connectivity.

Topologically, this mapping feature presents abundant shared sub-networks and edges between compound target sub-networks and core disease nodes, enabling multi-ingredient intervention to simultaneously act on the junctions of inflammatory and metabolic pathways rather than isolated single pathways. Notably, different ingredients act on the same core node via distinct binding sites or upstream and downstream links. For example, flavonoids tend to exert effects through the PPARγ pathway, while alkaloids mainly function via the AMPK pathway. Such divergence in action pathways forms the foundation of synergy rather than simple repetition.

The high correlation mapping between compound targets and disease network nodes verifies that multi-ingredients can intervene in the core regions of the inflammatory-metabolic network from multiple perspectives. It provides network-structural evidence for elaborating synergistic regulatory mechanisms in the following sections.

IV. MECHANISMS OF MULTI-INGREDIENT SYNERGISTIC REGULATION ON THE INFLAMMATORY-METABOLIC NETWORK

A. SYNERGISTIC INHIBITORY MECHANISM OF MULTI-INGREDIENTS ON INFLAMMATORY SIGNALING PATHWAYS

The synergistic inhibitory mechanism of multi-ingredients on inflammatory signaling pathways is embodied in multi-point intervention on upstream, midstream and downstream links of the NF-κB pathway by different ingredients.

Berberine suppresses the activity of IκB kinase, prevents phosphorylation and degradation of IκB protein, and blocks nuclear translocation of NF-κB subunits, thereby inhibiting transcriptional activation of downstream TNF-α and IL-6. Astragaloside IV reduces signal input activating the NF-κB pathway by interfering with the interaction between TLR4 and MyD88, forming an upstream-downstream complementary effect with berberine's downstream intervention.

Quercetin inhibits the assembly of the NLRP3 inflammasome by reducing mitochondrial reactive oxygen species, lowering the binding of NLRP3 with ASC, and decreasing maturation and release of IL-1β. This pathway is relatively independent of NF-κB, creating another entry point for anti-inflammatory regulation.

Various ingredients simultaneously suppress inflammatory signals at receptor recognition, signal transduction and inflammasome assembly links. Compared with single ingredients that only block one node, this multi-point synergistic mode can thoroughly cut off the cascade transmission of inflammation and stably maintain a chronic low-inflammatory state [5].

B. SYNERGISTIC REGULATORY MECHANISM OF MULTI-INGREDIENTS ON GLUCOSE AND LIPID METABOLIC PATHWAYS

The synergistic regulatory mechanism of multi-ingredients on glucose and lipid metabolic pathways centers on the AMPK and AKT/mTOR pathways.

Berberine elevates the intracellular AMP/ATP ratio to activate AMPK, which phosphorylates and inactivates acetyl-CoA carboxylase to boost fatty acid oxidation and suppress de novo fatty acid synthesis. Meanwhile, AMPK activation upregulates membrane translocation of GLUT4 to improve peripheral glucose uptake.

Astragaloside IV and ginsenosides tend to activate AKT via PI3K, restoring insulin signaling impaired by inflammation, and inhibit GSK3β to reactivate glycogen synthase and enhance hepatic glycogen synthesis.

Cross-talk exists between the two pathways: activated AMPK indirectly amplifies AKT signaling, while AKT positively regulates upstream kinases of AMPK. The two pathways form a synergistic amplification loop through this cross-link rather than functioning independently.

Organic acids such as mellitic acid activate PPARα to promote mitochondrial fatty acid oxidation, complementing the AMPK pathway in energy metabolism and simultaneously ameliorating disorders of glucose and lipid metabolism at multiple molecular layers [6].

C. SYNERGISTIC INTERVENTION MECHANISM ON INTERACTIVE NODES OF INFLAMMATORY AND METABOLIC PATHWAYS

The synergistic intervention mechanism targeting interactive nodes of inflammatory and metabolic pathways focuses on hub molecules including AMPK, NLRP3 and PPARγ that span both inflammatory and metabolic systems.

The effects of multi-ingredients on these interactive nodes do not occur in parallel, but form linkage effects through shared upstream signals or downstream effector molecules.

After activating AMPK, berberine not only improves fatty acid oxidation but also indirectly lowers precursor transcription of NLRP3 by inhibiting NF-κB, generating a synergistic

TABLE 2. Core interactive nodes of the inflammatory-metabolic network and their enriched pathways

Interactive Nodes	Node Degree Centrality	Main Enriched Pathways	Pathway Enrichment P-value	Functional Role in Network
AMPK	0.68	Energy metabolism, NF-κB pathway	2.3×10^{-6}	Hub linking metabolism and inflammation
NLRP3	0.61	NLRP3 inflammasome activation pathway	5.1×10^{-6}	Amplification node of inflammatory response
PPARγ	0.55	Adipocyte differentiation, macrophage polarization	1.8×10^{-5}	Conversion node of lipid metabolism and inflammation
AKT	0.59	PI3K/AKT/mTOR pathway	3.4×10^{-5}	Hub of insulin signal transduction
GSK3β	0.47	Glycogen synthesis pathway	7.2×10^{-5}	Downstream node of metabolic regulation

path transferring improvement from the metabolic end to the inflammatory end.

Quercetin directly inhibits NLRP3 starting from the inflammatory end, reducing IL-1β-mediated serine phosphorylation of insulin receptor substrate and restoring insulin signal transduction, forming another synergistic path.

The two paths converge at the AMPK-NLRP3 interactive node, producing superimposed rather than additive regulatory effects on the inflammatory-metabolic network.

Hypergeometric test is adopted to calculate the enrichment P-value to evaluate the statistical significance of core nodes in pathway enrichment analysis:

$$P = 1 - \sum_{i=0}^{k-1} \frac{C(M,i)\,C(N-M,n-i)}{C(N,n)}$$

Where N = total number of background genes; M = number of genes in target pathways; n = number of differential targets; i = number of differential targets enriched in target pathways. The main interactive nodes identified via network analysis are summarized in Table 2. The P-values of pathway enrichment for all nodes are below the significance threshold, verifying their core status in synergistic effects [7].

As visualized in Figure 1, the node degree centrality values of five core interactive nodes are presented in descending order, with a global average centrality of 0.58 marked by the dashed reference line. AMPK exhibits the highest degree centrality of 0.68, ranking first among all hub molecules, followed by NLRP3 (0.61) and AKT (0.59). PPARγ and GSK3β show relatively lower topological connectivity. All molecules except GSK3β possess centrality values above the average threshold, which further confirms that AMPK, NLRP3 and AKT act as the dominant coupling hubs connecting inflammatory signals and glycolipid metabolism pathways.

V. EXPERIMENTAL AND MULTI-OMICS VERIFICATION OF SYNERGISTIC REGULATORY EFFECTS OF HERBAL COMPOUND

A. VERIFICATION OF INFLAMMATORY AND METABOLIC INDICATORS IN ANIMAL MODELS

Verification of inflammatory and metabolic indicators in animal models is the critical step to validate hypotheses

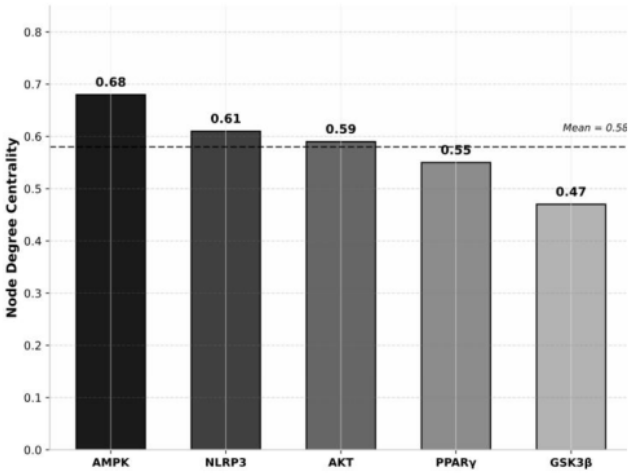

FIGURE 1. Bar chart of node degree centrality ranking of core interactive hubs in inflammatory-metabolic network

proposed by previous network analysis.

A type 2 diabetic rat model induced by high-fat diet combined with streptozotocin was established. Rats were randomly divided into model control group, low-dose compound group, high-dose compound group and positive drug control group, and administrated by gavage for 8 consecutive weeks. After treatment, fasting blood glucose, glycated hemoglobin and four blood lipid indicators were detected as metabolic markers; serum TNF-α, IL-6 and IL-1β were measured as inflammatory markers.

Detection results showed that fasting blood glucose and glycated hemoglobin levels in the high-dose compound group decreased significantly compared with the model control group, accompanied by synchronous reduction of serum inflammatory factors. The consistent improvement trend of metabolic and inflammatory indicators verified the synchronous regulatory effect predicted by network pharmacology.

Histopathological observation of liver tissues revealed alleviated hepatic steatosis and decreased inflammatory cell infiltration in compound-treated groups, further supporting the results of serum biochemical detection at the histological level.

Main detection results of inflammatory and metabolic indicators from each experimental group are listed in Table 3 for intuitive comparison. Data in Table 3 demonstrate that the high-dose herbal compound group achieves similar or even superior ameliorative effects compared with the positive control group [8].

The grouped bar chart in Figure 2 visually exhibits the numerical gaps of metabolic and inflammatory biomarkers among different groups, which is consistent with the statistical data listed in Table 3. The Model Control group holds the maximum value for all detected indicators, indicating severe glycolipid metabolic disorder and chronic inflammatory activation in diabetic rats. After intervention with the herbal compound, both the Low-Dose and High-Dose groups show

TABLE 3. Detection results of main inflammatory and metabolic indicators in all experimental groups

Detection Indicators	Model Control Group	Low-Dose Compound Group	High-Dose Compound Group	Positive Drug Control Group
Fasting blood glucose (mmol/L)	16.82	13.45	9.27	8.64
Glycated hemoglobin (%)	8.93	7.61	6.02	5.78
Triglyceride (mmol/L)	2.74	2.18	1.45	1.52
Serum TNF-α (pg/mL)	86.5	67.2	41.8	38.9
Serum IL-6 (pg/mL)	112.4	89.6	58.3	53.1

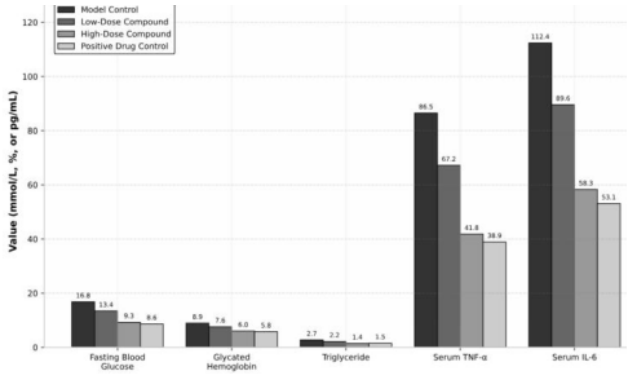

FIGURE 2. Comparison histogram of inflammatory and metabolic biomarkers among all experimental groups

obvious decreases in blood glucose, glycated hemoglobin, triglyceride, TNF-α and IL-6 in a dose-dependent manner. Moreover, the High-Dose Compound group presents similar ameliorative effects on inflammatory factors compared with the Positive Drug Control group.

B. CROSS-VERIFICATION VIA TRANSCRIPTOMICS AND METABOLOMICS DATA

Cross-verification via transcriptomics and metabolomics data aims to test whether core pathways predicted by network pharmacology actually change at the gene and small-molecule metabolite levels.

Liver tissues of rats in the high-dose compound group and model control group were subjected to transcriptome sequencing. Differentially expressed genes were screened for pathway enrichment analysis, and the AMPK and NF-κB signaling pathways ranked highest in significantly enriched pathways, highly consistent with network pharmacology predictions [9].

Simultaneous untargeted metabolomics detection revealed significant changes in serum free fatty acids, lactic acid and partial amino acid metabolites after compound administration, all annotated to fatty acid and amino acid metabolic pathways [10].

Pearson correlation coefficient was calculated to quantify the correlation between transcriptomic gene expression and metabolomic metabolite levels:

$$r = \frac{\sum(x_i - \bar{x})(y_i - \bar{y})}{\sqrt{\sum(x_i - \bar{x})^2 \sum(y_i - \bar{y})^2}}$$

Where x_i = gene expression level of corresponding sample; y_i = relative content of corresponding metabolite.

Calculation results indicated a moderate strong positive correlation between AMPK-related gene expression and fatty acid oxidation metabolites. The consistency across multi-omics layers provides solid experimental evidence for the hypothesis of multi-ingredient synergistic mechanisms [11].

C. CORRELATION EVALUATION BETWEEN NETWORK REGULATORY EFFECTS AND PHARMACODYNAMIC INDICATORS

Correlation evaluation between network regulatory effects and pharmacodynamic indicators integrates topological network analysis, animal experiments and multi-omics data into a unified evaluation framework, to judge whether core nodes predicted by network topology correspond to actual pharmacodynamic strength [12].

Sorting comparison between node degree centrality and improvement percentage of pharmacodynamic indicators shows that nodes with higher connectivity (AMPK, NLRP3) correspond to larger amelioration ranges of inflammatory and metabolic indicators, while low-connectivity peripheral targets match minor indicator improvements, presenting consistent ranking trends [13,14].

This consistency proves that topological parameters of network models can partially reflect actual pharmacodynamic contribution weight, providing methodological support for preliminary screening of high-potential active ingredients via network analysis.

Limitations still exist: some nodes with medium connectivity achieve better-than-expected pharmacodynamic effects in animal tests, indicating network models fail to fully incorporate non-linear interactions between ingredients.

Synthesizing network analysis and experimental verification, the synergistic regulatory mechanisms of herbal multi-ingredients on the inflammatory-metabolic network are systematically elucidated. The complete argument chain evolves from pathological coupling basis, ingredient-target mapping, synergistic pathway mechanisms to multi-omics experimental validation with consistent internal logic [15-17].

VI. CONCLUSION

The intervention effects of Chinese herbal compounds on type 2 diabetes rely on synchronous multi-node regulation of the inflammatory-metabolic network by multi-ingredients, rather than linear superposition of single-pathway effects.

Starting from the reciprocal causal coupling of glucose-lipid disorder and chronic inflammation, this paper systemat-

ically elaborates target mapping of herbal compounds, synergistic regulatory mechanisms on inflammatory/metabolic pathways and cross-layer intervention of interactive hub nodes, finally validated by in vivo animal tests and multi-omics data.

AMPK and AKT/mTOR pathways serve as core hubs linking inflammatory signals and glucose-lipid metabolism. Multi-ingredients regulate hub pathways via distinct targets to break the vicious cycle between insulin resistance and chronic inflammation.

This holistic network intervention model overcomes the limitations of single-target chemical drugs that fail to cover complex pathological networks, providing theoretical references for modern mechanistic research and clinical transformation of anti-diabetic herbal compounds.

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