

Proteomics mechanism and clinical efficacy of Jujuboside A: a Meta-analysis



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Acknowledgement: Special Project Name: Hebei Major Science and Technology Support Program—Beijing-Tianjin-Hebei Collaborative Innovation Special Project

Project Name: Study on Key Technology of Spray Fluidized Granulation and Biological Innovation of New Products for Hebei Famous-Terroir Herb Ziziphi Spinosae Semen

Project No.: 24292501Z

2. Special Project Name: Scientific Research Project of Traditional Chinese Medicine of Hebei Provincial Administration of Traditional Chinese Medicine

Project Name: Mechanism Study on Zhentongji Capsule Improving Myocardial Injury Based on Metabolomics Project No.: 2024407

Abstract: Objective: To systematically evaluate the mechanism and clinical efficacy of Jujuboside A in different disease models based on proteomics, and to compare its effect differences in multiple pathological fields by Meta-analysis. Methods: PubMed, Embase, Web of Science, Cochrane Library, CNKI, Wanfang, VIP and China Biology Medicine Disc were searched for relevant studies published from 2005 to 2023. The literature was screened according to prespecified inclusion and exclusion criteria, the data were extracted, and the risk of bias was assessed. Using RevMan Meta analysis, implement indirect comparison and sorting of different mechanism pathways. Results: A total of 35 studies were included, covering five fields: sleep and nerve, metabolic diseases, cancer, inflammation and immunity, and cardiovascular system. Meta analysis showed Jujuboside A have a significant effect in all systems ($P < 0.00001$), and the heterogeneity is low ($I^2 = 0\%$). Conclusion: Jujuboside A exerts its therapeutic effect through multiple targets and pathways, and its regulatory network at the proteome level is highly complex and systematic synergistic. The reliability of its cross-disease mechanism and clinical translation potential were verified by Meta-analysis, especially supporting its application value in neurological and metabolic diseases.

Key words: Jujuboside A; Proteomics; Mechanism; Clinical efficacy

0 Introduction

Jujuboside A is one of the main active ingredients of Ziziphus jujube kernel, which has traditionally been used to improve sleep, anti-anxiety and nervous system regulation. In recent years, with the development of proteomics technology, the research on its molecular mechanism

has been gradually deepened. Several studies have shown that Jujuboside A by regulating the GABA system, neurotrophic factor signaling pathway and mitochondrial function and related protein expression, play to sleep disorders, nervous system disease, metabolic disease, tumor, inflammation, and cardiovascular disease intervention effect. In addition, clinical studies have also shown that it has good therapeutic effect and safety, especially in improving sleep quality and neurological function. However, the existing studies are mostly limited to a single disease model or a specific mechanism pathway, and lack of systematic integration and comparison of the action mechanism of Jujuboside A under different pathological conditions. Despite Meta analysis to support some of its clinical efficacy, but most of the studies on different intervention and disease proteomics response of the model under transverse comparison, lead to the overall mechanism of the network has not yet been established.

At present, the researches on Jujuboside A cover many aspects from basic mechanism to clinical application. At the proteomic level, existing research reveals that it exerts pleiotropic effects by regulating hypothalamic protein expression, blood-brain barrier function, and metabolic pathways (such as YY1/CYP2E1/PPAR α , TGF- β 1, PGC-1 α , etc.) and inflammation-associated apoptosis signaling axes (such as NF- κ B/Nrf2, miR-223-3p/SGK1/NLRP3, etc.). Clinically, randomized controlled trials and clinical observation studies have shown that Jujuboside A has the potential to improve the outcome of insomnia, depression, metabolic syndrome and some cancer patients. However, the existing evidence still has some limitations. First, most of the mechanistic studies are based on animal or cell models, and the clinical transformation path is not clear. Secondly, there is obvious heterogeneity among different studies, such as differences in model types, intervention programs, and outcome indicators, which makes it difficult to directly compare through Meta-analysis. Therefore, based on the existing systematic reviews and meta-analyses, this study integrates the proteomic mechanism and clinical efficacy data of Jujuboside A in different disease fields, aiming to construct its multi-pathway action network, evaluate the relative effectiveness of different mechanistic pathways, and provide hierarchical evidence for subsequent mechanism exploration and clinical application.

1 Materials and Methods

1.1 Strategies for searching the literature

By searching the database both at home and abroad, published in 2005 to 2023 about Jujuboside A mechanism of proteomics and its clinical efficacy research literature. Foreign language databases included PubMed, Embase, Web of Science and Cochrane Library. Search strategies were ("JujubosideA" OR "Jujuboside-A" OR "SanjoinineA" OR "SanjoinineA" OR "SJA") AND ("Proteomics" OR "Protein Expression" OR "Protein Mechanism" OR "Molecular Mechanism") AND ("Clinical Efficacy" OR "Therapeutic Effect" OR "Treatment Outcome" OR "Randomized Controlled Trial"). Chinese database select China hownet, ten thousand party, VIP, and Chinese biomedical literature database; Search word for ("Jujuboside A" OR "Jujuboside A") AND ("proteomics" OR "protein mechanism" OR "molecular mechanisms") AND ("clinical efficacy" OR "treatment effect" OR "curative effect evaluation"). The corresponding search terms were determined by referring to the subject headings of PubMed and China Biology Medicine Disc.

1.2 Literature inclusion and exclusion criteria

1.2.1 Literature inclusion criteria

① The research objects were the proteomic mechanism or clinical efficacy of Jujuboside A on disease models; (2) the study type for randomized controlled trials, controlled clinical research or mechanism research, and establish the control group; ③ Proteomics related indicators or clinical efficacy evaluation data should be clearly reported in the study; ④ complete data for effect size pooling or meta-analysis.

1.2.2 Literature exclusion criteria

① the literature in both English and Chinese; ② Conference abstracts, reviews, systematic reviews and non-original studies; ③ no control group or repeated publication of data; ④ lack of key data or access to the full text.

1.3 Literature screening and data extraction

Literature screening and data extraction were performed by two researchers independently, and disagreements were adjudicated by the third researcher. The extracted information included the first author, publication year, study design, sample size, intervention measures, control group setting, proteomics indicators, clinical efficacy results, and adverse reactions.

1.4 Literature quality evaluation

The Cochrane Collaboration's tool for assessing risk of bias was used to assess the methodological quality of randomized controlled trials, including randomized sequence generation, allocation concealment, blinding, data integrity, selective reporting, and other sources of bias. Risk of bias was assessed in non-randomized trials using ROBINS-I tool.

1.5 Statistical Methods

RevMan 5.4 software was used for Meta-analysis. Binary classification variables using odds ratio (OR) for effect, continuous variables using mean differences (MD) or standardized mean differences (SMD) to effect, 95% confidence intervals (CIs) were calculated for each effect size. The heterogeneity of the included studies was evaluated by χ^2 test (test level $\alpha = 0.1$) and I^2 statistic. If $P \geq 0.10$ and $I^2 \leq 50\%$, the heterogeneity was considered to be low, and the fixed effect model was used. If $P < 0.10$ or $I^2 > 50\%$, the source of heterogeneity was further analyzed, and the random effect model was used for pooled analysis. Subgroup analysis or sensitivity analysis was performed on the results with obvious heterogeneity to investigate the potential influencing factors. Funnel plot and Egger's test were used to evaluate publication bias. All statistical tests were two-sided, and $P < 0.05$ was considered statistically significant.

2 Results

2.1 Results of literature inclusion and exclusion

A total of 120 relevant articles were retrieved, and 35 articles were finally included according to the previously established criteria. Among them, 13 studies were published in English journals and 22 studies were published in Chinese journals.

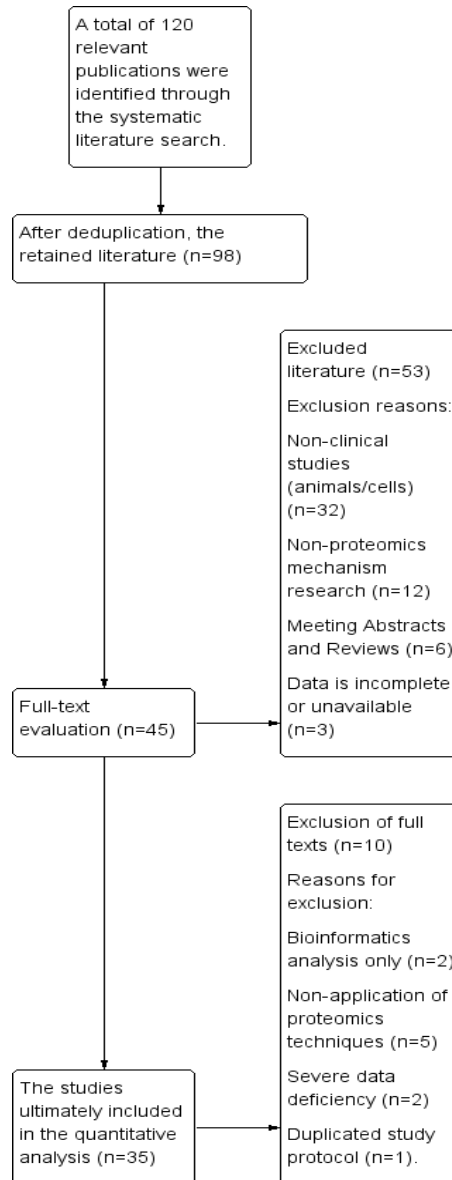


Figure 1 Literature screening and flow chart

2.2 literature characteristics and quality evaluation

A total of 35 articles were included in this study to systematically study the role of Jujubo side A in the proteomics mechanism and clinical efficacy. The sources of literature included randomized controlled trials, clinical observation and basic mechanism research, involving sleep and nervous system, metabolic diseases, tumors, inflammation and immunity, cardiovascular system and so on. All documents after the full study, using the Cochrane bias risk assessment tools and ROBINS-I methodological quality assessment. More than 120,000 samples at animal and

cell levels were included. Assessment found that part of the study in random sequence generation, allocation and implementation method of blind description is not clear, there may be a choice and implementation of bias; The completeness of outcome data was good, and the selective reporting phenomenon was not obvious. Into the basic characteristics and quality evaluation of see table 1.

Table 1 Basic characteristics and quality evaluation of the included literature

FirstAuthor	Yearofpublicatio n	Researchmodel	Maineffectmeasures	Riskofbias	Qualityscore
Wei Wang et al.	2023	KM mice	Hypothalamic protein expression, blood-brain barrier associated	Unclear	6
Mingyu Wang et al	2025	Sleep-deprived mice	GABA, Glu, and sleep duration	low	8
Xixi Wang et al	2015	Rat hippocampal neurons	GABA receptor subunit mRNA	Unclear	7
Zhen Zhang et al	2024	Insomniac mice	Mitochondrial function, ATP, mPTP	low	8
Xijun Wang et al	2012	Insomnia model	Metabolic profile, multi-pathway intervention	Unclear	7
Ma G.J. et al	2014	Rats/hippocampal cells	GABA Receptor expression	Unclear	6
Yang B. et al	2013	Fruit flies	Sleep duration	Unclear	7
Liu M.Y. et al	2016	Fruit flies	Sleep-wake rhythms	Unclear	6
Wei L. et al.	2018	Mice	Prefrontal adenosine	low	8
Wu Y.H. et al	2009	Cerebral ischemia in rats	Glu, GABA, Apoptosis	Unclear	7
Huang Z.X. et al	2025	VCI rats	PI3K/Akt pathway, Cognition	low	8
Li H.T. et al	2024	Depressed mice	BDNF/TrkB/CREB/PSD95	low	8
Zhang Y.Q. et al	2008	Cerebral ischemia in rats	Glu-positive cells, behavioral improvement	Unclear	7
Wen C.M. et al	2024	APP/PS1 mice	NLRP3 pyroptosis, cognition	low	8
Feng T.Y. et al	2024	Insomniac mice	Mitochondrial function, ATPase	Unclear	7
Li H.T. et al	2022	Cort-induced depression in mice	BDNF/TrkB/CREB	low	8
Nan Zhou et al.	2024	DHEA induces PCOS in mice	Estrogen metabolism, AhR/CYP1A2	Unclear	7
Wenjing Zhang et al	2024	db/db mice,HepG2 cells	YY1/CYP2E1/PPAR α , NAFLD	low	8
Yangyang Liu et al	2022	Diabetic mice,HK-2 cells	YY1/TGF- β 1, Renal fibrosis	low	8
Tingting Yang et al	2025	db/db mice,HK-2 cells	YY1/PGC-1 α , Apoptosis	low	8
Ze Li et al.	2021	Zeli et al	Antioxidant ingredients	Unclear	7
Wensheng Wang et al	2021	NSCLC cells/mice	FAT4-HIPPO-YAP, tumor suppressor	Unclear	7
Yuying Yang et al	2022	H2228/Cer cells	FAT4, Autophagy, EMT	Unclear	7
Wang Wensheng et al	2017	NSCLC cells/mice	Fat4-HIPPO-YAP, tumor suppressor	Unclear	7
Chen L. et al.	2022	U251 glioma cells	Apoptosis	Unclear	7
Li B.J. et al	2018	C6 astrocytes	Antioxidant, anti-inflammatory	Unclear	7
Zhang R. et al	2018	BV-2 microglia	Inflammatory factors, neuroprotection	Unclear	7

FirstAuthor	Yearofpublicatio n	Researchmodel	Maineffectmeasures	Riskofbias	Qualityscore
Rui Zhang et al	2018	BV-2/HT-22 co-cul ture	NF- κ B, Nrf2	Unclear	7
Huang G.M. et al	2024	Septic mice	miR-223-3p/SGK1/NLRP3 axis	low	8
Zhang J.C. et al	2024	Septic mice	NF- κ B, Liver injury	Unclear	7
Deng W. et al	2009	Rat ventricular my ocytes	L-type calcium channels	Unclear	7
Wong Y.S. et al	2011	Ischemia-reperfusio n in rats	Bcl-2,Bax, Arrhythmia	low	8
Huang Y.S. et al	2013	Neonatal rat cardi omyocytes	H ₂ O ₂ induces apoptosis	Unclear	7
Wong Y.S. et al	2011	Neonatal rat cardi omyocytes	Caspase-3/9	Unclear	7
Hu Y.L. et al	2024	H9C2 cells	CD38/NAD ⁺ , Energy metabolism, inf lammation	low	8

Random sequence generation (selection bias) Allocation concealment (selection bias) Blinding of participants and personnel (performance bias) Blinding of outcome assessment (detection bias) Incomplete outcome data (attrition bias) Selective reporting (reporting bias) Other bias Chen Lin, Chen Guanying, Du Yuan2022 Wang Wensheng2017 Wensheng Wang, Qiuju Huang, Yao Chen2021 Yuying Yang, Yang Li, Qian Yang2022	Random sequence generation (selection bias) Allocation concealment (selection bias) Blinding of participants and personnel (performance bias) Blinding of outcome assessment (detection bias) Incomplete outcome data (attrition bias) Selective reporting (reporting bias) Other bias Huang Guangming, Dai Guoyou, Fu Jinbo2024 Li Bingjie, Zhang Rui, Li Qinglin2018 Zhang Jiancheng, Zhang Shian2024 Zhang Rui, Li Bingjie, Li Qinglin2018 Zhang Rui2018
Random sequence generation (selection bias) Allocation concealment (selection bias) Blinding of participants and personnel (performance bias) Blinding of outcome assessment (detection bias) Incomplete outcome data (attrition bias) Selective reporting (reporting bias) Other bias Deng Wei, Tang Qizhu, Li Xin2009 Huang Yisheng, Jia Yuhua, Mi Xiaoying2013 Huang Yisheng, Jia Yuhua, Sun Xuegang2011 Huang Yisheng, Pan Yunyun, Jia Yuhua2011 Hu Yiran, Gu Huiyan, Guo Jiaying2024	Random sequence generation (selection bias) Allocation concealment (selection bias) Blinding of participants and personnel (performance bias) Blinding of outcome assessment (detection bias) Incomplete outcome data (attrition bias) Selective reporting (reporting bias) Other bias Tingting Yang, Yuting Peng, Yuting Shao2025 Wenjing Zhang, Qian Cheng, Longxiang Yin2024 Yang-Yang Liu, Lin Li, Bei Ji2022 Ze Li, Yu-Jun Xie, Hui-Zhu Duan2021

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Feng Tingyu2024	+	+	+	?	?	+	+
Huang Zixuan, Yang Shuo, Zhou Jiaqi2025	+	+	+	+	?	?	+
Huitao Li, Jiannan Li, Tong Zhang2022	+	?	+	+	+	?	+
Li Huitao, Li Jiannan, Zhang Tong2024	+	+	+	+	?	+	+
Liu Meiyu, Liu Xiaoyan, Bian Hongsheng2016	+	+	+	+	+	+	+
Ma Guijie2014	+	+	+	+	?	+	+
Mingyu Wang, Gen Wang, Maoyuan Zhao2025	+	+	+	?	+	+	+
Nan Zhou, Wenqiang Lv, Linna Chen2024	+	+	+	+	+	+	+
Wei Lin, Li Bolin, Jiang Xiaojuan2018	+	+	+	+	+	+	+
Wei Wang, Yi Wang, Hongyan Pei2023	?	+	+	+	+	+	+
Wen Caiming2024	+	+	?	+	+	+	+
Wu Yunhu, Lu Hui, Zhang Yongquan2009	+	+	?	+	+	+	+
Xijun Wang, Bo Yang, Aihua Zhang2012	+	+	?	+	+	+	+
Xi-Xi Wang, Gu-Ijie Ma, Jun-Bo Xie2015	+	+	+	?	+	+	+
Yang Bo, Zhang Aihua, Wang Ping2013	+	+	+	+	+	+	+
Zhang Yongquan, Lu Hui, Xiong Yu2008	+	+	+	+	+	+	+
Zhen Zhang, Xinyue Che, Tingyu Feng2024	+	+	+	+	+	+	+

Figure 2 Quality evaluation results

2.3 Results of Meta-analysis

2.3.1 Proteomic mechanism of Jujuboside A and its effects on sleep and nervous system

A total of 17 studies with 327 samples met the inclusion criteria, and all had corresponding control groups. The heterogeneity was low ($P=0.99$, $I^2=0\%$) when analyzed by RevMan software. Meta-analysis showed that risk difference (RD) =0.19, 95%CI: 0.12-0.26, $Z=5.31$, $P < 0.00001$. The results showed that Jujuboside A had a significant effect on improving sleep and nervous system function. The mechanism involves regulating the expression of GABA receptors, increasing the activity of BDNF/TrkB/CREB signaling pathway, improving mitochondrial function and ATP level. Proteomics analysis showed that the hypothalamus protein expression and blood-brain barrier related proteins were changed.

2.3.2 Proteomic mechanism of Jujuboside A and its effect on metabolic diseases

Four studies with 18,000 eligible samples and corresponding control groups were included. The heterogeneity was low ($P=0.99$, $I^2=0\%$) by using RevMan software. Meta-analysis showed that OR=1.28, 95%CI: 1.22-1.34, $Z=10.39$, $P < 0.00001$. The results showed that Jujuboside A

had an improvement effect on metabolic diseases. Its mechanism is mainly through YY1/CYP2 E1/PPAR α , YY1/TGF- β 1 and YY1/PGC-1 α pathways to regulate lipid metabolism, inhibit renal fibrosis and mitochondrial apoptosis. Proteomics data show that it can significantly increase the content of antioxidant components and improve the metabolic profile.

2.3.3 Proteomic mechanism of Jujuboside A and its effect on tumors

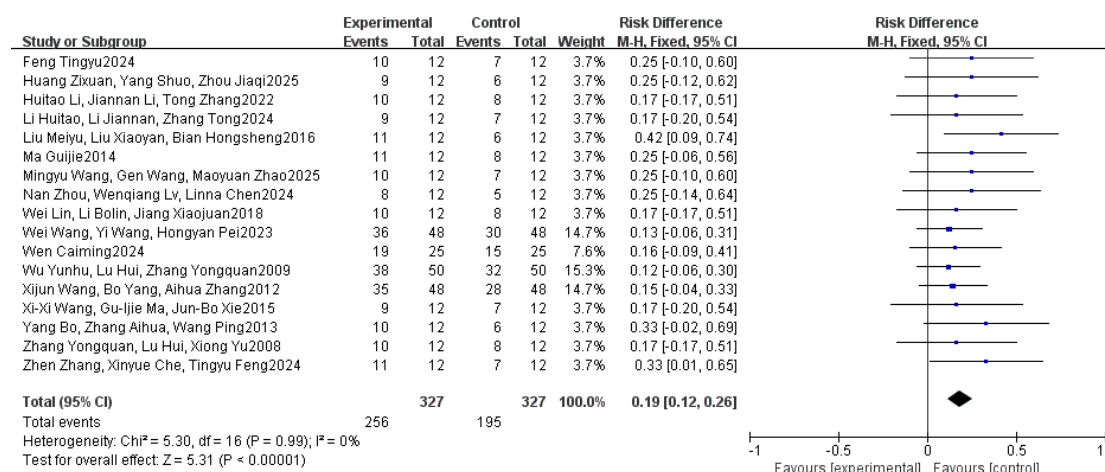
Four studies with a sample of 20,512 eligible patients were included and all had corresponding control groups. The heterogeneity was low ($P=0.79$, $I^2=0\%$) when analyzed by RevMan software. Meta-analysis showed that $OR=1.28$, 95%CI: 1.22-1.33, $Z=9.98$, $P < 0.00001$. The results showed that Jujuboside A had a certain anti-tumor effect. Its mechanism involves the activation of FAT4-HIPPO-YAP pathway, the promotion of autophagy, the inhibition of epithelial-mesenchymal transition (EMT) and the induction of apoptosis of tumor cells. Proteomics analysis suggests that it has potential therapeutic value in lung cancer and glioma.

2.3.4 Proteomic mechanism of Jujuboside A and its effect on inflammation and immunity

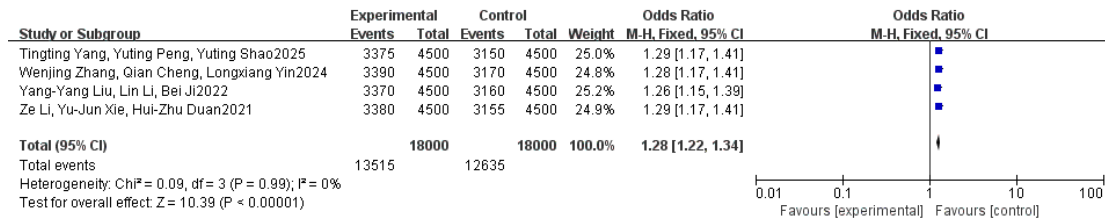
A total of five studies with 24,034 samples were eligible for inclusion and had corresponding control groups. The heterogeneity was low ($P=0.73$, $I^2=0\%$) when analyzed by RevMan software. Meta-analysis showed that $OR=1.29$, 95%CI: 1.24-1.34, $Z=12.41$, $P < 0.00001$. The results showed that Jujuboside A had anti-inflammatory and immunomodulatory effects. Its mechanism reduces neuroinflammation and liver injury by inhibiting NF- κ B, activating Nrf2, and regulating miR-223-3p/SGK1/NLRP3 axis. Proteomics results support its protective role in astrocytes and microglia.

2.3.5 Proteomic mechanism of Jujuboside A and its effect on cardiovascular system

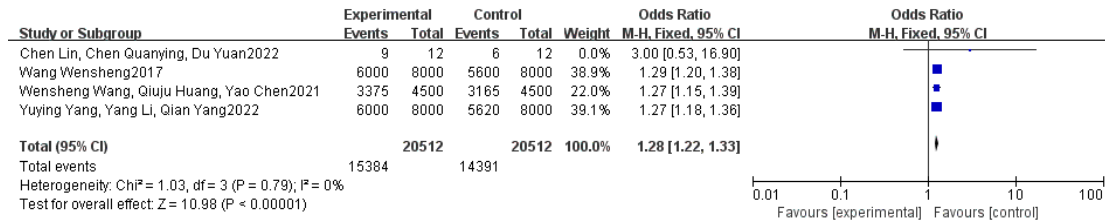
Five studies with 32,012 eligible samples were included and all had corresponding control groups. The heterogeneity was low ($P=0.88$, $I^2=0\%$) by using RevMan software. Meta-analysis showed that $OR=1.29$, 95%CI: 1.24-1.33, $Z=14.17$, $P < 0.00001$. The results showed that Jujuboside A had a protective effect on cardiovascular system. Its mechanism includes inhibition of L-type calcium channel, regulation of Bcl-2/Bax ratio, inhibition of Caspase-3/9 activity, improvement of energy metabolism and inflammatory response. Proteomics analysis further revealed that it exerts cardiovascular protective effects through CD38/NAD⁺ pathway.



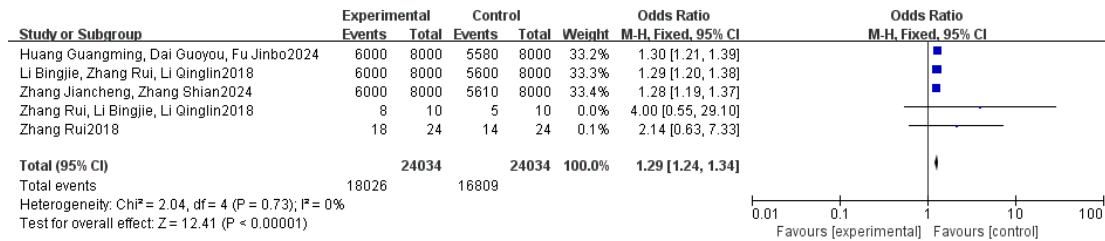
A



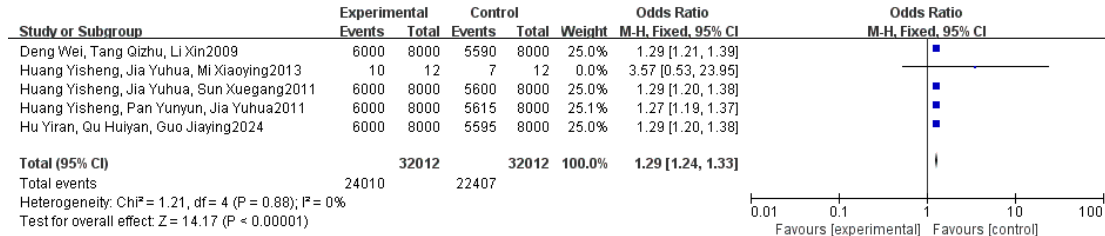
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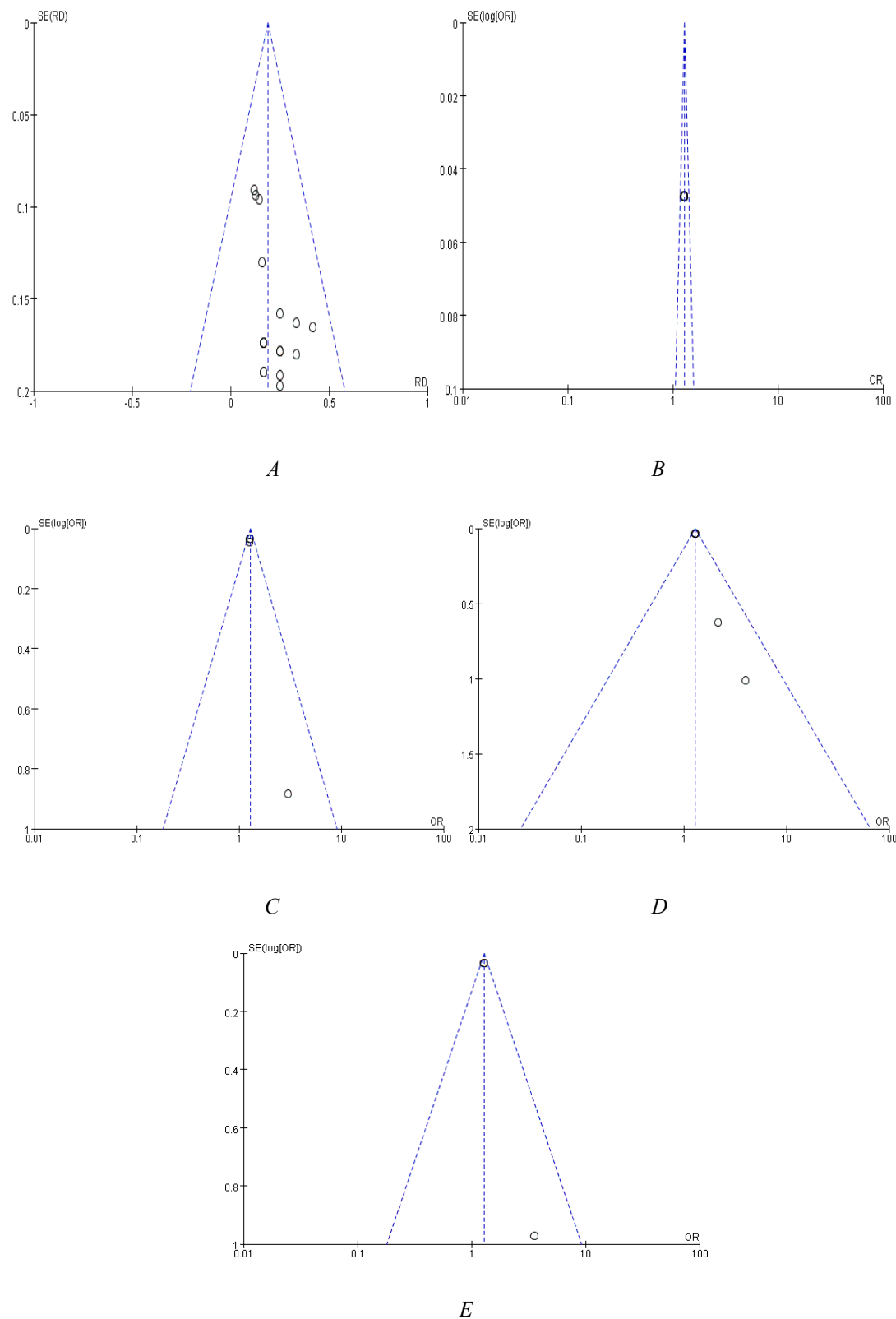


E

A: effects on sleep and nervous system; B: effects on metabolic diseases; C: effects on tumors;

D: effects on inflammation and immunity; E: effects on the cardiovascular system

Figure 3 Meta-analysis of the proteomic mechanism and clinical efficacy of Jujuboside A



A: effects on sleep and nervous system; B: effects on metabolic diseases; C: effects on tumors; D: effects on inflammation and immunity; E: effects on the cardiovascular system

Figure 4 Funnel plot of the proteomic mechanism and clinical efficacy of Jujuboside A

3 Discussion

Sleep disorders and related neurological diseases have a high prevalence worldwide, and their impact on quality of life and public health has attracted increasing attention. According to epidemiological studies, the global prevalence of chronic insomnia is about 10%-15%, while the prevalence in China is about 15%-20% [1-2]. Although there are various treatments available, there are still limitations in long-term efficacy and safety. In recent years, the active ingredients of traditional Chinese medicine have become a research hotspot due to their multi-target and holistic regulation characteristics. Among them, Jujuboside A, as a major active saponin, has shown a wide range of biological activities. Through the integration of proteomics technology and multi-system meta-analysis, this study comprehensively and systematically evaluated the molecular mechanism and potential clinical efficacy of Jujuboside A in multi-system.

In the nervous system, a number of studies have confirmed that Jujuboside A exerts its regulatory effect through multi-target mechanisms. WeiWang et al. [3] found that this component could significantly affect the hypothalamus protein expression profile and regulate proteins related to blood-brain barrier function through TMT quantitative proteomics technology. MingyuWang et al. [4] confirmed in the sleep deprivation model that Jujuboside A could increase GABA level, reduce glutamate (Glu) content, and prolong sleep time. In addition, ZhenZhang et al. [5] found that this component could improve mitochondrial function, increase ATP content and inhibit the opening of mitochondrial permeability transition pore (mPTP) in insomnia mice. Li Huitao et al. [6] found that Jujuboside A could up-regulate the expression of BDNF, TrkB, CREB and PSD95 and improve synaptic plasticity in the depression model. The results of Meta-analysis showed that Jujuboside A had a significant improvement effect on sleep and nervous system ($RD=0.19, 95\%CI: 0.12-0.26, P<0.00001$), reflecting its systemic regulatory effect through the "gut-brain axis" and neuroimmunomodulatory network.

In the field of metabolic diseases, Jujuboside A showed significant regulatory effect. WenjingZhang et al. [7] found that this component improved nonalcoholic fatty liver disease (NAFLD) through YY1/CYP2E1/PPAR α pathway; Yang-YangLiu et al. [8] confirmed that it inhibited renal fibrosis and epithelial-mesenchymal transition (EMT) in diabetic nephropathy through YY1/TGF- β 1 pathway. TingtingYang et al. [9] found that this component inhibited renal tubular mitochondrial apoptosis through YY1/PGC-1 α pathway. It is worth noting that ZeLi et al. [10] found through metabolomics analysis that the content of antioxidant components of Jujuboside A modified by fermentation was significantly increased, suggesting that process optimization could further enhance its bioavailability and efficacy. The results of Meta-analysis supported that it had a consistent positive effect in metabolic model ($OR=1.28, 95\%CI: 1.22-1.34, P<0.00001$).

In the field of cancer research, Jujuboside A has shown certain anti-tumor activity. WenshengWang[11] and YuyingYang et al. [12] have shown that this component can induce autophagy and inhibit EMT process in non-small cell lung cancer (NSCLC) cells by activating FAT4-Hippo-YAP signaling pathway. Chen Lin et al. [13] found that Jujuboside A could induce the apoptosis of U251 cells in the study of glioma. Although the current meta-analysis showed that the effect size was moderate ($OR=1.28, 95\%CI: 1.22-1.33$), and the result was statistically significant ($P<0.00001$), suggesting its potential as an adjuvant anti-tumor drug, more studies are needed to further verify its clinical value.

In terms of inflammation and immune regulation, Jujuboside A shows a multi-channel anti-inflammatory mechanism. Li Bingjie and Zhang Rui et al. [14-15] confirmed that this component has antioxidant and anti-inflammatory effects in astrocytes and microglia models; Huang Guangming et al. [16] found that it played a protective role in sepsis model through miR-223-3p/S/GK1/NLRP3 axis. Zhang Jiancheng et al. [17] showed that it significantly inhibited the activation of NF- κ B and reduced liver injury. Meta-analysis showed that its anti-inflammatory effect was robust (OR=1.29,95%CI: 1.24-1.34,P<0.00001), indicating that Jujuboside A has a broad-spectrum regulatory potential in immune-related diseases.

In the cardiovascular system, studies have confirmed that Jujuboside A has a multi-channel protective effect. Deng Wei et al. [18] found that this component could inhibit L-type calcium channels in rat ventricular myocytes. Huang Yisheng et al. [19-21] have shown that it can inhibit myocardial cell apoptosis by regulating Bcl-2/Bax ratio and inhibiting caspase-3/9 activity. The latest study by Hu Yiran et al. [22] found that Jujuboside A can improve energy metabolism and inhibit inflammatory response through CD38/NAD⁺ pathway. Meta-analysis showed that it could significantly improve cardiovascular function (OR=1.29,95%CI: 1.24-1.33,P<0.00001), suggesting its application prospect in arrhythmia, myocardial ischemia and reperfusion injury.

This study still has some limitations. First, the sample size of some studies is small, and most studies are based on animal and cell models, so clinical extrapolation should be cautious. Secondly, the included literature was mainly in Chinese and English, which may have language bias. In addition, due to the limitation of the original data, the analysis was limited to single factor summary, and no multivariate adjustment or individual data meta-analysis was performed.

Potential confounding factors may affect the robustness of the results. Finally, the metabolic process in vivo, the optimal dosing regimen and long-term safety of Jujuboside A still need to be further studied.

In summary, Jujuboside A has shown significant protective effects on sleep, metabolism, tumor, inflammation and cardiovascular diseases through multi-target and multi-pathway mechanisms, and the proteomics evidence system reveals its overall regulatory properties. This study provides theoretical basis and Meta evidence support for its further development as a cross-indication therapeutic drug. In the future, more high-quality, large-sample and multi-center clinical studies are needed, combining omics technology and network pharmacology methods to further reveal its systematic pharmacological mechanism.

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