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A Disseminated Intravascular Coagulation Animal Model: How Compound Danshen Dripping Pills Work and What They Do

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Abstract: Purpose: Using transcriptome analysis, we want to learn how compound Danshen dripping pills (CDDP) affect diffuse intravascular coagulation (DIC) and what mechanisms CDDP may work by. Research Tools and Procedures: We carried out DIC animal models with various inducers and studied the impact of CDDP on many parameters, including survival rate, blood flow to the hepatic and gastric fundi, aberrant prothrombin time (PT), fibrinogen (FIB) concentration, inflammatory factors, and the damage index for the liver and kidneys. After that, confirmation of the primary target genes was done using whole-blood transcriptome sequencing. The results showed that CDDP increased the efficiency of glutamic pyruvic transaminase and glutamic oxaloacetic transaminase, improved blood flow in the stomach and liver, increased PT and FIB values, decreased the elevated serum levels of interleukin-10 and tumor necrosis factor-alpha, and increased blood urea nitrogen and creatinine. Additionally, it improved the survival rate of the animals used in the study. According to research using whole-blood transcriptome sequencing, CDDP may control inflammatory response in the immune system, oxidative stress, activation and aggregation of platelets, and cell death in DIC. The model animals' aberrant expression of Sqstml, Ctsd, Mylk2, and Nfkbib was further enhanced by CDDP, as demonstrated by quantitative polymerase chain reaction (qPCR). Results: CDDP protects primary organs in DIC models by reducing inflammatory factor expression, increasing organ blood flow, and correcting coagulation anomalies. Not only that, but CDDP enhanced the outcome of DIC animal models by boosting the expression of important genes associated with the illness, namely Sqstml and Nfkbib.

Keywords: Various terms such as microcirculation, disseminated intravascular coagulation, the Sqstml gene, transcriptomics, and compound Danshen dripping tablet are used.

INTRODUCTION

Microthrombuses develop all over the place and systemic coagulation is activated in disseminated intravascular coagulation (DIC), a condition of acquired coagulation dysfunction. [1] One of the most dangerous outcomes for patients suffering from sepsis, tumors, acute leukemia, placental abruption, or trauma, it happens as a response to several disorders. Due to its high death rates and vulnerability to organ failure, DIC is difficult to detect and has a bad prognosis when treated. [2] in The coagulation system becomes activated and microvascular system gets damaged when pathogenic agents do this. the third Furthermore, coagulation factors have a role in

the breakdown and consumption of platelets and coagulation factors leading to hemorrhage and thrombosis. According to reports, a significant number of patients in the intensive care unit (ICU) have signs of DIC, which may lead to an increased death rate. The most common cause of DIC is infection. [6] The new coronavirus causes the acute infectious illness known as coronavirus disease 2019 (COVID-19), which impacts several organs and systems. Those two In addition,

a number of mechanisms, including inflammation, immunology, cell

the establishment of a clotting-inflammation-immune network, adhesion, and platelet activation. [4] The core feature of DIC is the presence of unregulated

COVID-19 patients in critical care often present with abnormal coagulation function. Multiple systems, including coagulation, inflammation, and the immune complement system, are involved in coagulation dysfunction in COVID-19 individuals, according to studies. [9] Infections may progress to DIC in critically sick individuals, leading to unfavorable health consequences. Depending on the treatment of underlying conditions, heparin or low-molecular-weight heparin is now recommended as the first-choice medicine for DIC according to worldwide treatment recommendations. Citations [10,11] Nevertheless, a number of studies have shown that heparin has no discernible impact on patients' long-term survival rates and carries a large risk of severe side effects including bleeding. Consequently, the creation of efficient methods for treating DIC is a pressing and unfulfilled therapeutic need.

For the treatment of coronary heart disease (CHD), the China Food and Drug Administration has authorized compound Danshen dripping tablet (CDDP) during the last quarter of a century. Many studies have shown that CDDP can alleviate myocardial ischemia-induced angina symptoms by improving blood circulation, decreasing blood viscosity, protecting endothelial cells, inhibiting leukocyte adhesion and inflammation, and optimizing myocardial energy metabolism. [12] Moreover, prior research has shown that CDDP has pharmacological actions such enhancing microcirculation, preventing platelet adhesion and aggregation, acting as an antioxidant and anti-inflammatory, and safeguarding endothelial functions. [13] Myocardial ischemia and DIC have similar clinical and physiological processes, such as inflammation, impaired coagulation function, and platelet activation. This suggests that the regulatory mechanism by which CDDP protects against DIC and CHD is similar as well. Thus, the purpose of this study was to examine the effectiveness of CDDP in treating DIC in two separate animal models and to investigate, using transcriptomics as a starting point, the potential mechanism of CDDP's treatment of DIC. The ultimate goal is to provide evidence supporting CDDP's use in treating DIC and to provide a safe and effective option for patients suffering from clinical DIC.

Materials and Methods

Animals

Specific pathogen-free (SPF) male Kunming mice, weighing 20 ± 2 g, were purchased from the Beijing Weitong Lihua Experimental Animal Technology Co., Ltd. (animal certificate number: 110011110698978). SPF male Sprague–Dawley rats, weighing 200 ± 20 g, were purchased from the Beijing Vital River Laboratory Animal Technology Co., Ltd (animal certificate number: 110011211104397472). The animals were fed using the Tianjin Tasly Proud Pharmaceutical Co., Ltd. animal barrier system (facility license: SYXK (Tianjin) 2017-0006). They were adapted to feeding for 3 days, during which their weight, head, and torso conditions, and activity levels were monitored. The present study was approved by the Committee on Animal Experimentation of the Tasly Academy (ethics approval code: TSL-IACUC-2020-19, TSL-IACUC-2020-20).

Apparatus and reagents

The tool

The following instruments were used: a laser speckle blood flow imaging system (moorFLPI-2), a semi-automatic coagulation analyzer (Siddhi Scientific Instruments, LG-PABER-I), a microplate reader (TECAN, Infinite M200), an automatic biochemical analyzer (Hitachi 7020), a fragment analyze biological analyzer (Thermo, FSv2-CE), a gene sequencing instrument (Shenzhen Huada, DNBSEQ-T7), a qPCR instrument (Analytik Jena, qTOWER3G), and a chemiluminescence imager (Shanghai Qianxiang, ChemiScope6200).

Chemicals and substances

The drug and reagents used were: CDDP (TASLY, 190117), nadroparin calcium injection (Aspen, 5325B), high molecular dextran (H20M10B88790), ulcerose (T20100310), sodium chloride injection (2012174C), lipopolysaccharide (LPS; SIGMA, 0000081275), prothrombin time detection kit (Taizhou Zhongqin, STY20101-41-9), and fibrinogen (FIB) determination kit (Taizhou Zhongqin, STY20401-39-5). Rat interleukin-10 (IL-10) enzyme-linked immunosorbent assay (ELISA) kit (Shanghai Enzyme-linked, Nov 2020), rat tumour necrosis factor- alpha (TNF-α) ELISA kit (Shanghai Enzyme-linked, Nov 2020), glutamic pyruvic transaminase (GPT) test kit (Nanjing Jiancheng, 20210305), glutamic oxaloacetic transaminase (GOT) test kit (Nanjing Jiancheng, 20210304), creatinine (Cr) test kit (Nanjing Jiancheng, 20210304), TransZol (Beijing TransGen ET111-01), reverse transcription kit (Takara, RR047A).

Research techniques

How the Danshen dripping tablet composition affects the survival rate of rats stimulated with lipopolysaccharide? Intraperitoneal injection of LPS into rats allowed researchers to reproduce the mouse model of DIC. There were three sets of animals used as models: those given CDDP-H (1660 mg/kg), those given CDDP-L (830 mg/kg), and those given nadroparin calcium (500 IU/kg). In order to mimic the DIC model, 35 mg/kg of LPS was intraperitoneally administered into all groups of mice except the control group. After modeling, mice in the model group received 10 mL/kg of pure water; mice in the CDDP group received the indicated doses of CDDP intragastrically; and mice in the nadroparin calcium group received 500 IU/kg of nadroparin calcium subcutaneously. At 72 hours post-modeling, we measured the survival rate of each group of experimental animals.

Effect of compound Danshen dripping pill on dextran-induced microcirculatory disturbance

The rat model of DIC microcirculation disorder was established by injecting 10% dextran T500 into the tail vein. The rats were divided into the control, model, CDDP-H (830 mg/kg), CDDP-L (415 mg/kg), and nadroparin calcium (500 IU/kg) groups. Different doses of CDDP were administered by gavage

1.5 h before the model was replicated. Blood perfusion of the rat liver and gastric fundus was detected using the Moor FLPI-2 laser speckle blood flow imaging system 10 min before dextran T500 injection and 5, 15, and 30 min after dextran T500 injection to investigate the effect of CDDP on microcirculation disorder.

Effect of compound Danshen dripping pill on lipopolysaccharide-induced animal model

The DIC model was replicated by intraperitoneally injecting the rats with LPS. The rats were divided into the control, model, CDDP-H and CDDP-L, and nadroparin calcium groups. Except for the control group, rats in all other groups were intraperitoneally injected with 30 mg/kg LPS to replicate the DIC model. Rats in the control and model groups were intragastrically administered 10 mL/kg of pure water immediately after modeling. Rats in the CDDP group were intragastrically administered 415–835 mg/kg CDDP immediately after modeling. Rats in the nadroparin calcium group were subcutaneously injected with 500 IU/kg nadroparin calcium, immediately after modeling. The rats in each group were sacrificed 6 h after the model was replicated; blood and organ tissues were collected from the abdominal cavity after anesthesia, and the samples were processed according to the instructions. Hematological examination (prothrombin time [PT] and FIB), inflammatory factor detection (IL-10 and TNF-α), and pathological examination of the liver and kidneys were performed.

Transcriptomics detection and validation

The rats in the control, model, and CDDP-H groups (n = 5 rats in each group) were anesthetized with intraperitoneal injection of 20%, 4 mL/kg urethane administered 6 h after the model was replicated. Blood was collected from the abdominal aorta and placed in a PAXgene Blood RNA tube according to the instructions provided in the kit. Total RNA was extracted, and transcriptome sequencing was performed. The DEseq2 software and Metacore website were used to quantify the aforementioned genes and analyze them based on gene expression (correlation, principal component analysis, and differential gene screening). Gene Ontology (GO) enrichment analysis, Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway enrichment analysis, and protein interaction network analysis were performed on differential gene data in selected samples.

For qPCR, the RNA samples from experimental animals were reverse-transcribed according to the instructions provided in the kit. The PCR primers were designed using Primer 5.0 software. Quantitative real-time (qRT)-PCR was performed using the SYBR Green fluorescent dye. The amplification curve was obtained by real-time monitoring of the PCR using the dissolution curve. The Ct-value of the target gene was calculated using the amplification curve, and the gene expression changes were quantitatively calculated using the $2^{-\Delta\Delta Ct}$ formula.

Statistics

Microsoft Excel was used to analyze and process the data. The experimental data obtained from each group are expressed as mean ± standard deviation. The two-sample equal variance t-test was used to examine the significance between the groups, and $P < 0.05$ was considered statistically significant.

RESULTS

Effect of compound Danshen dripping pill on the survival rate of lipopolysaccharide-induced model animals

The survival rates of rats in the CDDP-L, CDDP-H, and nadroparin calcium groups were 8.35%, 37.5%, 87.5%, and 25%, respectively [Figure 1A]. The results suggested that CDDP improved the survival rate of LPS-induced model rats in a dose-dependent manner.

Effect of compound Danshen dripping pill on dextran-induced microcirculatory disturbance

Preadministration of 415 mg/kg CDDP significantly increased the 5-min and 15-min hepatic blood flow and 30-min gastric fundus blood flow in DIC rats following 10% dextran T500 modeling ($P < 0.05$). Preadministration of 830 mg/kg CDDP significantly increased the 5-min and 15-min hepatic blood flow and the 5-min and 30-min gastric fundus blood flow after modeling in DIC rats ($P < 0.05$). These findings suggested that CDDP plays a therapeutic role in DIC microcirculation disorder by improving the microcirculation in internal organs and increasing blood perfusion of organs [Figure 2a-c].

Effect of compound Danshen dripping pill on lipopolysaccharide-induced rat model

Effect of compound Danshen Dripping Pill on coagulation function in lipopolysaccharide-induced model rats

The prothrombin time (PT) in the model group was significantly prolonged (model vs. control; $P < 0.01$) and the FIB level was significantly decreased ($P < 0.01$), suggesting LPS-induced coagulation abnormalities in model rats. After the model was replicated, different doses of CDDP improved LPS-induced coagulation dysfunction. Notably, the CDDP-H group showed significant improvement than that of the model group ($P < 0.01$), demonstrating an effect comparable to that of the nadroparin calcium group [Figure 1B].

Effect of compound Danshen dripping pill on inflammatory factors in lipopolysaccharide-induced model animals

Compared with the control group, the model group demonstrated a significant increase in serum IL-10 and TNF-α levels ($P < 0.05$). Different doses of CDDP improved the LPS-induced abnormal increase in inflammatory factors ($P < 0.05$), which was equivalent to the effect of nadroparin calcium, suggesting that CDDP exerts an inhibitory effect on inflammatory factors in LPS-induced model animals [Figure 1C].

Effect of compound Danshen dripping pill on liver and kidney function of lipopolysaccharide-induced animal model

Compared with the control group, the model group demonstrated an abnormal increase in GPT and GOT activities and blood

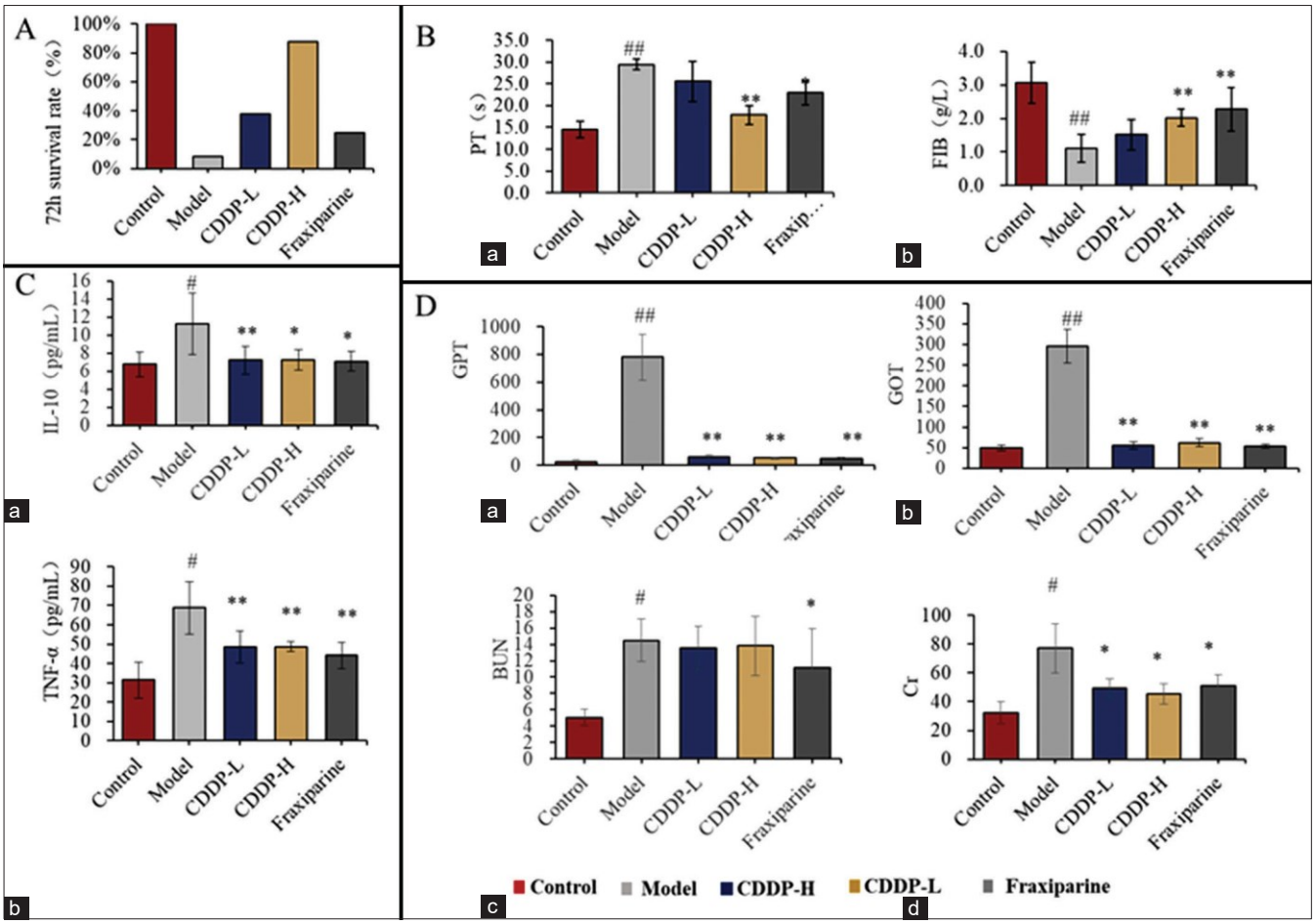

Figure 1: Lipopolysaccharide-induced disseminated intravascular coagulation model assay. (A) The 72 h survival rate of model mice (n = 8). (B; a and b) Effect of compound Danshen dripping pill on PT value and FIB levels in model rats (n = 6). (C; a and b) Effect of compound Danshen dripping pill on inflammatory factors in model rats (n = 6). (D; a-d) Effect of compound Danshen dripping pill on hepatic and kidney injury in model rats (n = 6) in comparison with control rates. $^{\#}P < 0.05$, $^{\#\#}P < 0.01$; comparison with the model group, $^{*}P < 0.05$, $^{**}P < 0.01$. CDDP: Compound Danshen dripping pills

urea nitrogen (BUN) and creatinine (Cr) levels in the model group ($P < 0.01$), suggesting that the model rats suffered a certain degree of liver and kidney damage. Different doses of CDDP significantly reduced the activities of GPT and GOT ($P < 0.01$) and the levels of BUN and Cr ($P < 0.01$) in rat plasma, similar to the effect exerted by nadroparin calcium. These results suggested that CDDP exerts a protective effect against LPS-induced liver and kidney injury in model animals [Figure 1D].

Histopathological observation of the effects of CDDP on lipopolysaccharide-induced animal model.

Hematoxylin and eosin staining revealed initial pathological damage 6 h following the intraperitoneal injection of LPS in animals in the model group. Different levels of CDDP reduced the initial pathological damage caused by LPS-induced DIC in the lungs, liver, and kidneys [Figure 3].

In the control group, the alveolar septum wall was thin, and the cells were normal, whereas, in the model group, the alveolar septum wall was thick, with alveolar septal capillary dilation congestion (▲), which increased around the blood vessels, along with edema (★). In the control group, the liver cells were arranged in plates, the central vein was filled with red blood cells, and the portal area vessels and bile ducts were arranged normally; whereas the model group exhibited hepatocyte vacuolar degeneration (×), partial nuclear lysis, and hepatic sinusoid dilatation and congestion (on, without inflammatory cell infiltration. In the model group, no abnormalities were observed in the glomeruli, but there was an increase in red blood cells and congestion in the renal interstitial capillary (ap. Compared with the model and control group, the CDDP group exhibited reduced pulmonary edema and pulmonary perivascular space, decreased hepatocyte vacuolar degeneration, and improved renal interstitial capillary congestion.

Transcriptome sequencing analysis and verification

Transcriptome sequencing analysis

We used the screening conditions of $|\log_2 FC| \geq 1$ and $q \leq 0.05$ and found 543 common and significantly differentially expressed genes in the control group, model group, and CDDP group [Figure 4a].

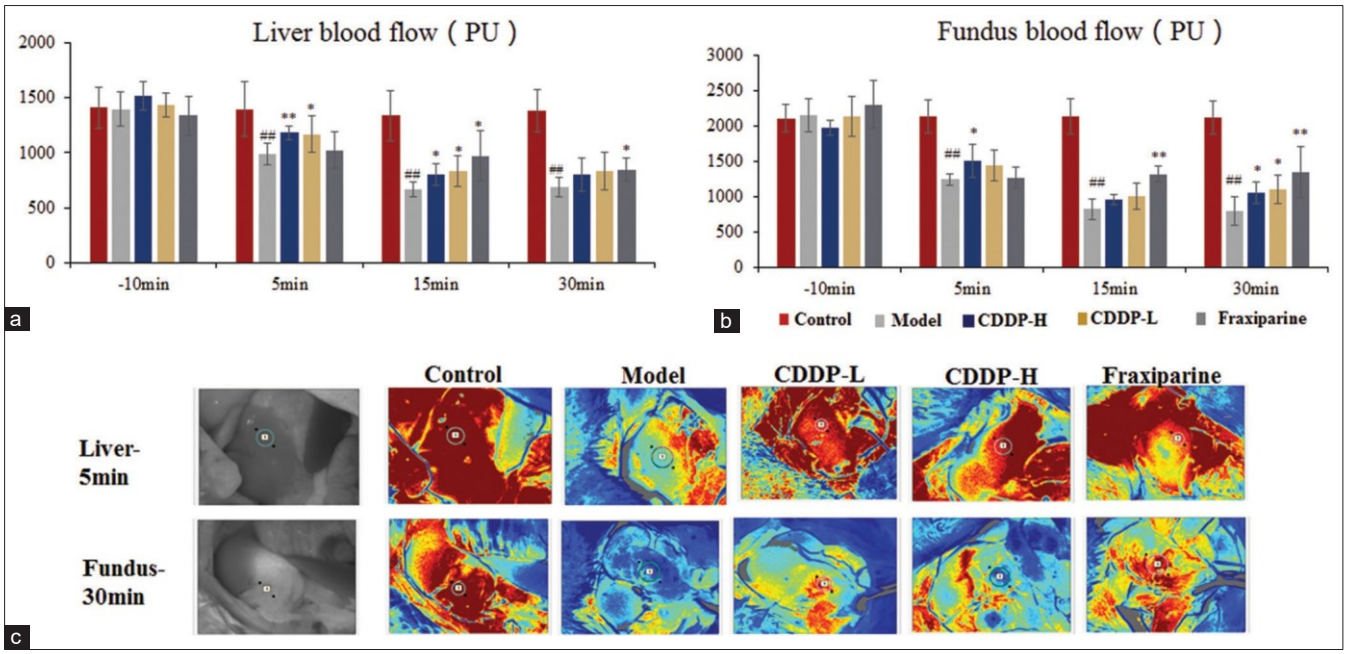

Figure 2: Dextran-induced microcirculatory disturbance model assay (a) Liver blood flow in different groups. (b) Liver blood flow in different groups. (c) Liver and gastric fundus blood flow between 0 and 30 min after modeling in each group, $^{\#}P < 0.05$, $^{\#\#}P < 0.01$; comparison with the model group, $^{*}P < 0.05$, $^{**}P < 0.01$ ($n = 6$). CDDP: Compound Danshen dripping pills

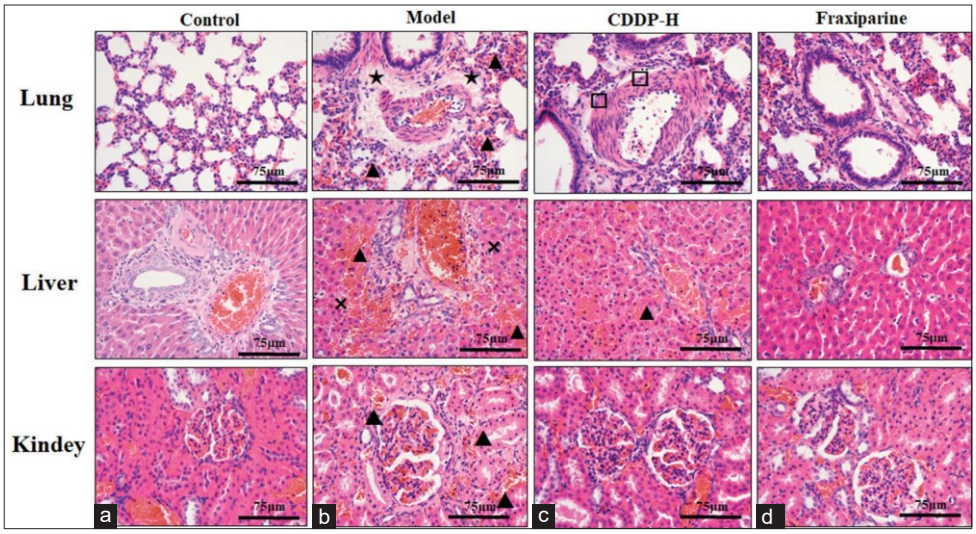

Figure 3: Hematoxylin and eosin staining in different groups(×400). The HE staining of the organ tissues were observed under a 400x microscope. Hematoxylin and eosin staining in different groups. In the lung, the model group exhibits alveolar septum thickening, alveolar septum capillarydilation congestion (▲) and increased edema around the blood vessels (★). In the liver, the model group exhibits hepatocyte vacuolar degeneration(×), partial nuclear lysis, and hepatic sinusoid dilatation and congestion (▲). In the kidney, the model group exhibits increased in red blood cells andcongestion in the renal interstitial capillary (▲), Pulmonary edema was slightly reduced and perivascular space was reduced (□). a: Control group;b: Model group; c: CDDP-H group; d: Fraxiparine group. CDDP: Compound Danshen dripping pills

Differential gene enrichment analysis

The Gene Ontology (GO) enrichment analysis and KEGG pathway enrichment analyses were performed on the 543 genes. The results demonstrated that CDDP primarily participated in the regulation of immune inflammatory response, complement system, oxidative stress response, COVID-19-related coagulation disorders, platelet activation, aggregation, and apoptosis. It has been suggested that CDDP confers therapeutic potential against DIC by regulating the immune complement system, exerting anti-inflammatory properties, promoting coagulation and platelet activation, countering antioxidative stress, and inhibiting apoptosis.

Gene ontology enrichment analysis

We used the Dr. Tom online system to analyze the biological processes, cellular components, and molecular functions of the

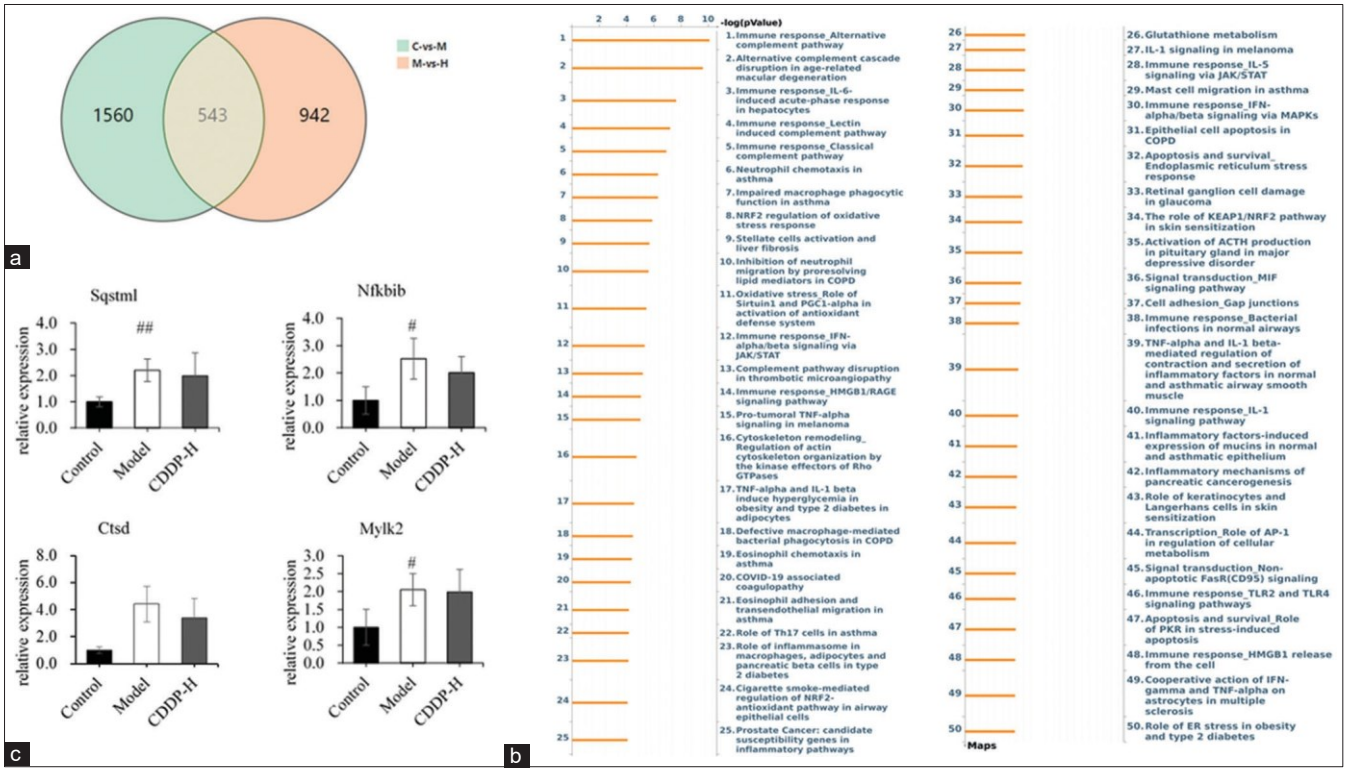

Figure 4: Whole blood transcriptome sequencing differential gene analysis and verification. (a) Differential gene VEEN map (control vs. model vs. CDDP-H groups); (b) Pathway maps enrichment analysis of differential genes (Q-value ranked top 50); (c) Results of quantitative polymerase chain reaction assay (n = 5), in comparison with the control group. $^{\#}P < 0.05$, $^{\#\#}P < 0.01$. CDDP: Compound Danshen dripping pills

differentially expressed genes. The results demonstrated that the GO terms enriched by differentially expressed genes involved 2727 biological processes, 462 cellular components, and 804 molecular functions. The biological processes primarily included inflammatory response, immune system process, response to lipopolysaccharides, innate immune response, neutrophil response, and antioxidative stress. Cellular components primarily involved the cytoplasm, cell fluids, ribosomes, soluble fibrin, and mitochondria. The molecular functions included protein labeling, ubiquitin protein ligation, cytokine receptor activation, IL-1 receptor activation, complement component C3b binding, and Toll-like receptor binding. These results indicated a strong connection between differentially expressed genes and the coagulation–immune system, suggesting that CDDP exerts its therapeutic effect on DIC through the above pathways.

KEGG enrichment analysis

The KEGG pathway enrichment analysis was performed on the differentially expressed genes using the MetaCore database (https://portal. genego. com/). The top 50 pathways with the smallest Q-values, that is, the most significant enrichment, were selected for display. In addition, the top 50 pathways were found to be the immune response complement pathway, IL-6-induced acute phase response of hepatocytes, neutrophil chemotaxis, oxidative stress response, thrombotic microangiopathy, high mobility group box 1 signaling pathway, TNF-α signaling pathway, IL-1 β signaling pathway, and COVID-19-related coagulation disorders. Most of these pathways were related to the immune response and coagulation system, suggesting potential pathways for the treatment of DIC using CDDP [Figure 4b].

Analysis of key targets and pathways of CDDP in the treatment of DIC

The results of the transcriptome analysis, *P* values of differential gene enrichment, and functions of the enriched pathways were used to further classify the differentially expressed genes. The related targets and corresponding pathways of CDDP in the DIC model rats were analyzed. Comprehensive analysis revealed that CDDP exerts a therapeutic effect on DIC by affecting the oxidative stress response and acting on apoptosis-related pathways. In addition, the analysis revealed that CDDP exerted therapeutic potential against COVID-19 by affecting thrombosis [Figure 5].

Validation of transcriptomics analysis results

The results of transcriptome analysis revealed that the key targets of CDDP in the treatment of DIC were primarily enriched in immune coagulation, oxidative stress, platelet activation, inflammasome, and apoptosis-related pathways. Based on literature research, four key genes, namely, *Sqstml*, *Ctsd*, *Mylk2*, and *Nfkbib*, were selected for qPCR verification, and the effect of CDDP on LPS-induced model animals was preliminarily observed. The results demonstrated that, compared with the control group, the model group significantly increased expression of four target genes, *Mylk2*, *Nfkbib* ($P < 0.05$), *Ctsd,* and *Sqstml* ($P < 0.01$), in the whole blood of

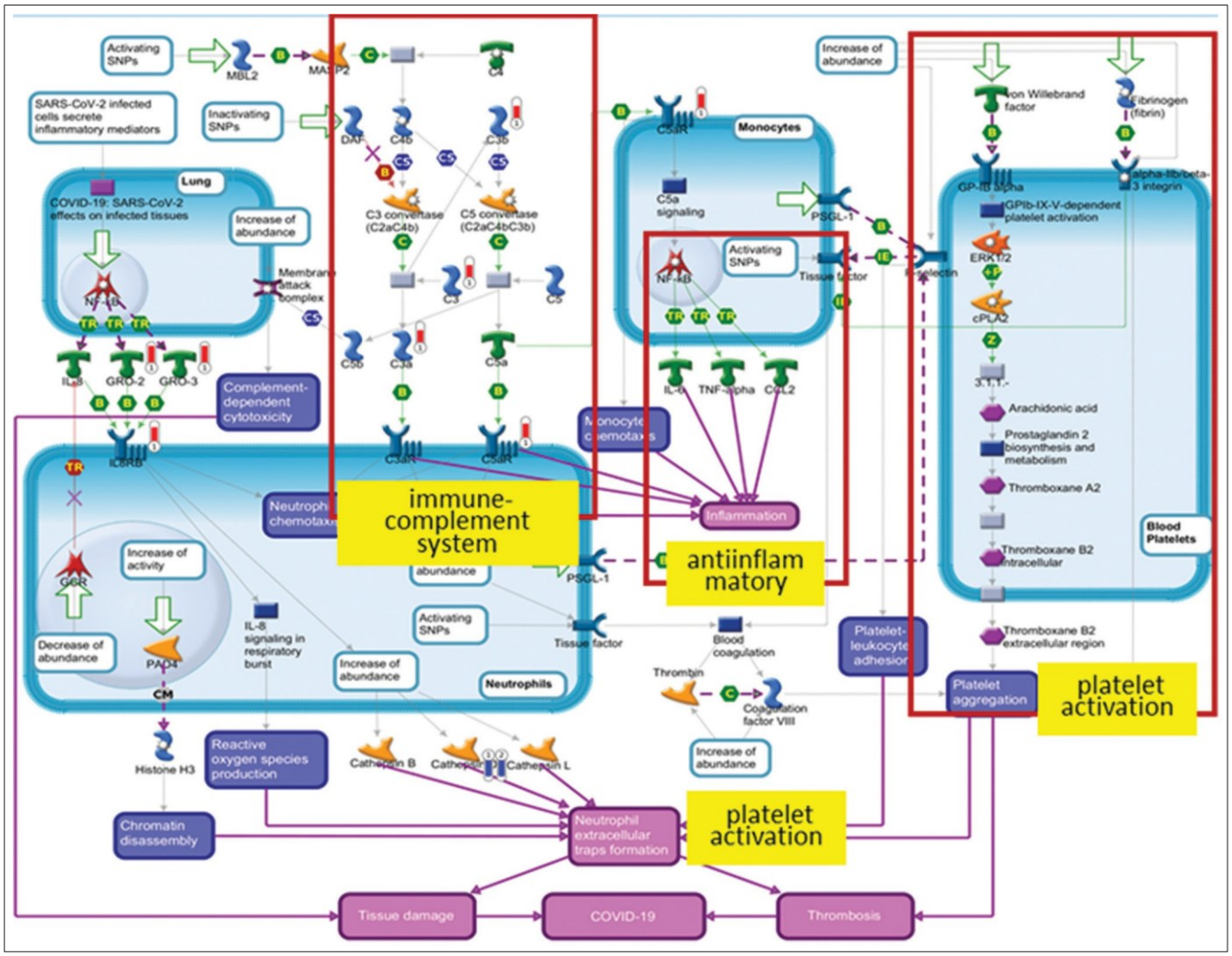

Figure 5: Coagulation disorder-related pathways

the model rats 6 h after model replication. CDDP inhibited the overexpression of *Mylk2*, *Nfkbib*, *Ctsd*, and *Sqstml* to varying degrees. The results of qRT-PCR were consistent with those of transcriptome sequencing [Figure 4c].

Discussion

In DIC, an acquired coagulation condition, microthrombuses develop all over the place and systemic coagulation is activated. A number of biological systems, including those involved in coagulation, innate immunity, inflammation, complement, and fibrinolysis, are disrupted by the disorder's severe microcirculatory abnormalities. (2, 3). According to clinical research, DIC symptoms are seen by 10%-30% of intensive care unit (ICU) patients, leading to an increased death rate. The main cause of DIC is infection. When it comes to treating infectious disorders, traditional Chinese medicine offers some distinct benefits. [14] Here, we looked at how CDDP affected the rate of survival in an animal model that was induced with LPS. The findings showed demonstrated the survival rate of LPS-induced model mice was significantly enhanced by a single oral dosage of CDDP at varied doses. The main clinical symptom of DIC has been described as organ failure due to the production of microthrombi in various organ microvessels. [15] By injecting 10% dextran T500 into the tail vein of rats, we were able to replicate an animal model of DIC microcirculatory disorder. After 5-30 minutes of model replication, we observed that a single oral dose of CDDP increased organ blood flow and continuously improved blood perfusion in the gastric fundus and liver, suggesting that CDDP may have therapeutic effects on DIC by improving microcirculation in these model animals.

The etiology and clinical manifestations of DIC in LPS-induced rats are similar to those in humans suffering from clinical infections. A hallmark of this paradigm is the development of microthrombi and extensive coagulation. [16] To examine CDDP's therapeutic potential, we used an LPS-induced DIC rat model in this investigation. Prolonged PT during consumptive hypocoagulation and secondary is seen in the majority of DIC patients, according to clinical

findings.
time periods including fibrinolysis (hypercoagulation). Another inflammatory biomarker that shows the greatest plasma coagulation factor level is FIB, a glycoprotein produced by liver cells. 17 and 18 Our results show that CDDP enhances normal coagulation function in LPS-induced model animals, as it prolongs PT and reduces LPS-induced plasma FIB level in rats. Additionally, cytokines including TNF and IL-1 facilitated coagulation activation, fibrinolysis injury, and organ damage in the LPS-induced DIC animal model. [15] A single oral dose of CDDP considerably reduced the levels of inflammatory cytokines like IL-10 and TNF-α in DIC model rats, as well as the activity of markers for liver and kidney damage like GPT and GOT, as well as the levels of BUN and Cr in their plasma, according to the results. The results indicated that CDDP prevents damage to the main organs by reducing inflammatory factor expression. Furthermore, the early pathological damage to the lungs, liver, and kidneys produced by LPS-induced DIC was ameliorated by CDDP, as shown by HE pathological staining. These findings provide promising evidence that CDDP may be useful in the treatment of DIC in animals by enhancing microcirculatory function and protecting important organs by reducing inflammatory factor expression.
After that, we looked at potential CDDP targets in DIC therapy by sequencing the whole-blood transcriptome of animals across several groups. In LPS-induced DIC model rats, CDDP showed therapeutic potential via immunological modulation, anticoagulation, antiinflammation, inhibition of platelet activation, and cell death, according to the GO and KEGG enrichment analyses of the differentially expressed genes. We confirmed the target genes using qPCR: Sqstml, Ctsd, Mylk2, and Nfkbib. Our selection was based on experimental findings and a literature study. This prediction approach was confirmed to be feasible since the target genes were considerably elevated in the CDDP group compared to the model group, which was in agreement with the projected outcomes. CDDP skewed the expression of the innate immune regulating factor Sqstml. In addition, it is thought of as a predictor of outcome in cases of serious infections in humans and in animal models generated by LPS. The year 19 Activated nuclear factor-kappaB (NF-κB) is linked to several organ dysfunctions, and it is known to have a significant role in endothelial cell damage and apoptosis brought on by severe infections. Patients with sepsis may have a better chance of surviving if the NF-κB activity is inhibited. Among the many roles it plays in the heart and in the activation and aggregation of platelets, Mylk2, an affiliate of the myosin light chain kinase family, is mentioned in reference [20]. References [21,22] After ischemia and hypoxia, autophagy activates Ctsd, leading to lysosomal dysfunction. Cell apoptosis involves both internal and extrinsic processes, to which it contributes at various stages. [23] The Ctsd may also initiate cell death by directly activating caspase 3. This research found that CDDP improved the aberrant expression of

The blood of rats that were induced DIC by LPS included Sqstml, Ctsd, Mylk2, and Nfkbib.
In this work, we found that CDDP increased blood flow to the primary organs of rats with DIC, which protected those organs from damage. Also, it blocks cell death, controls inflammatory factor expression, decreases coagulation malfunction in DIC, and blocks platelet activation pathways. Supporting the expression of important genes linked to disease development, including Sqstml and Nfkbib, may be the underlying mechanism. In conclusion, CDDP has promise for enhancing DIC prognosis and creating a more efficient treatment plan.

CONCLUSIONS

This study showed that CDDP may have protective effects in DIC model animals by improving organ blood flow and coagulation abnormalities and inhibiting the expression of inflammatory factors. The therapeutic effects of CDDP on DIC model animals may be achieved by increasing the expression of key genes related to DIC, including *Sqstml* and *Nfkbib*, thereby improving the prognosis of model animals. This study only preliminarily explored the efficacy and mechanism of CDDP in the treatment of DIC, and the key targets and pathways of action should be further clarified and verified to explain the mechanism of action of CDDP in the treatment of DIC further clearly.

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Nil.

Conflicts of interest

The authors assert that the study was conducted without any commercial or financial affiliation that may pose a conflict of interest.

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