

A Traditional Chinese Medicine Extract, Drug, and Detection Method

TECHNICAL FIELD

[0001] The present invention relates to the field of traditional Chinese medicine, particularly to a traditional Chinese medicine extract, drug, and their detection method.

BACKGROUND OF THE INVENTION

[0002] Viral pneumonia is a disease caused by upper respiratory viral infections that spread downwards, leading to pulmonary inflammation and impaired lung gas exchange function. This disease can occur throughout the year, but is most commonly seen in winter and spring, and can occur in outbreaks or sporadic cases. Clinically, it is mainly characterized by fever, headache, body aches, dry cough, and pulmonary infiltration. Pneumonia caused by influenza viruses is the most common, while other pathogens such as respiratory syncytial virus (RSV), adenovirus, and parainfluenza virus have also attracted widespread attention.

[0003] Viral infections primarily manifest as interstitial lung lesions. Initially, they affect ciliated columnar epithelial cells, followed by invasion of other respiratory cells, including alveolar cells, mucus gland cells, and macrophages. The virus replicates within the cells and then releases infectious viral particles to infect neighboring cells. Infected ciliated cells may undergo degenerative changes, including granular degeneration, vacuolization, cell swelling, and nuclear condensation, leading to necrosis and disintegration. Cellular debris accumulates in the airways, obstructing the small airways, causing airway swelling. The alveolar septa show significant inflammatory responses, accompanied by infiltration of lymphocytes and macrophages, occasionally with plasma cells, neutrophils, and edema. Necrosis and bleeding fibrin thrombi may be present in the pulmonary capillaries, and eosinophilic hyaline membranes may be observed in the alveoli. Severe

infections may lead to pulmonary edema, consolidation, bleeding, lung parenchyma necrosis, and atelectasis.

[0004] Influenza viruses and respiratory syncytial virus are the most common viruses causing upper respiratory infections. Influenza virus belongs to the family Orthomyxoviridae and is an RNA virus. Based on antigenic differences in viral nucleoprotein and matrix protein, it is classified into types A, B, and C. Type A influenza virus has a high mutation rate and strong virulence. H1N1/FM1 is a mouse-adapted strain of influenza virus A used to simulate pulmonary infection damage. The influenza A virus initiates infection by binding hemagglutinin to cell surface receptors containing sialic acid on respiratory epithelial cells. After entering the cells, the viral genome begins transcription and replication. A large number of progeny viral particles are produced, which spread through the respiratory mucosa and infect other cells, thereby triggering a cytokine storm, leading to systemic inflammatory response, acute respiratory distress syndrome (ARDS), shock, and multiple organ failure. Respiratory syncytial virus, belonging to the family Paramyxoviridae, is an RNA virus. Its pathogenesis involves the interaction between the virus and the host cell injury, inflammation, body fluid and local immune responses, and hyper-reactivity.

[0005] Currently, various data and clinical use have confirmed that traditional Chinese medicines (TCMs) exhibit significant antiviral efficacy with a broad antiviral spectrum and minimal toxic side effects. Furthermore, many of these medicines also have antipyretic, anti-inflammatory, and other effects, providing multiple actions against viral infections, such as reducing fever duration, controlling the spread of inflammation, and promoting inflammation resolution. This multi-pathway, multi-target approach proves effective in combating viral infections. Due to the diversified active ingredients in TCMs during treatment, viruses are less likely to develop drug resistance, giving traditional Chinese medicine a clear advantage in treating viral infectious diseases and offering promising

clinical applications.

BRIEF SUMMARY OF THE INVENTION

[0006] The aim of this invention is to address the shortcomings of the prior art by providing a Traditional Chinese Medicine (TCM) extract with antiviral activity. The extract is characterized in that, by weight ratio, the TCM extract is made from the following ingredients: *Magnoliae Officinalis Cortex* 1-100 parts, *Arecae Semen* 1-100 parts, *Amomum tsaoko* Crevost & Lem. 1-100 parts, *Ephedrae Herba* 1-100 parts, *Armeniacae Semen Amarum* 1-100 parts, *Notopterygii Rhizoma et Radix* 1-100 parts, *Zingiberis Rhizoma* 1-100 parts, *Pogostemonis Herba* 1-100 parts, *Eupatorium fortunei* Turcz. 1-100 parts, *Atractylodis Rhizoma* 1-100 parts, *Poria cocos* 1-100 parts, *Atractylodis Macrocephalae Rhizoma* 1-100 parts, *Gypsum Fibrosum* 1-100 parts, *Crataegi Fructus* 1-100 parts, *Massa Medicata Fermentata* 1-100 parts, *Hordei Fructus Germinatus* 1-100 parts, *Pheretima* 1-100 parts, *Vincetoxicum pycnostelma* Kitag. 1-100 parts, *Dryopteridis Crassirhizomatis Rhizoma* 1-100 parts, and *Lepidium apetalum* seeds 1-100 parts.

[0007] Further, the TCM extract is made from the following ingredients: *Magnoliae Officinalis Cortex* 1-80 parts, *Arecae Semen* 1-80 parts, *Amomum tsaoko* Crevost & Lem. 1-80 parts, *Ephedrae Herba* 1-60 parts, *Armeniacae Semen Amarum* 1-60 parts, *Notopterygii Rhizoma et Radix* 1-80 parts, *Zingiberis Rhizoma* 1-60 parts, *Pogostemonis Herba* 1-80 parts, *Eupatorium fortunei* Turcz. 1-60 parts, *Atractylodis Rhizoma* 1-80 parts, *Poria cocos* 1-160 parts, *Atractylodis Macrocephalae Rhizoma* 1-120 parts, *Gypsum Fibrosum* 1-80 parts, *Crataegi Fructus* 1-50 parts, *Massa*

Medicata Fermentata 1-80 parts, Hordei Fructus Germinatus 1-60 parts, Pheretima 1-80 parts, Vincetoxicum pycnostelma Kitag. 1-80 parts, Dryopteridis Crassirhizomatis Rhizoma 1-60 parts, and Lepidium apetalum seeds 1-80 parts.

[0008] Furthermore, the TCM extract is made from the following ingredients: Magnoliae Officinalis Cortex 30-50 parts, Arecae Semen 20-30 parts, Amomum tsaoko Crevost & Lem. 30-50 parts, Ephedrae Herba 20-30 parts, Armeniacae Semen Amarum 20-30 parts, Notopterygii Rhizoma et Radix 30-50 parts, Zingiberis Rhizoma 30-50 parts, Pogostemonis Herba 30-50 parts, Eupatorium fortunei Turcz. 20-30 parts, Atractylodis Rhizoma 30-50 parts, Poria cocos 120-150 parts, Atractylodis Macrocephalae Rhizoma 80-100 parts, Gypsum Fibrosum 30-50 parts, Crataegi Fructus 20-30 parts, Massa Medicata Fermentata 30-50 parts, Hordei Fructus Germinatus 20-30 parts, Pheretima 30-50 parts, Vincetoxicum pycnostelma Kitag. 30-50 parts, Dryopteridis Crassirhizomatis Rhizoma 20-30 parts, and Lepidium apetalum seeds 30-50 parts.

[0009] Furthermore, the TCM extract is made from the following ingredients: Magnoliae Officinalis Cortex 50 parts, Arecae Semen 30 parts, Amomum tsaoko Crevost & Lem. 50 parts, Ephedrae Herba 30 parts, Armeniacae Semen Amarum 30 parts, Notopterygii Rhizoma et Radix 50 parts, Zingiberis Rhizoma 50 parts, Pogostemonis Herba 50 parts, Eupatorium fortunei Turcz. 30 parts, Atractylodis Rhizoma 50 parts, Poria cocos 150 parts, Atractylodis Macrocephalae Rhizoma 100 parts, Gypsum Fibrosum 50 parts, Crataegi Fructus 30 parts, Massa Medicata Fermentata 50 parts, Hordei Fructus Germinatus 30 parts, Pheretima 50 parts, Vincetoxicum pycnostelma Kitag. 50 parts, Dryopteridis Crassirhizomatis Rhizoma

30 parts, and *Lepidium apetalum* seeds 50 parts.

[0010] Additionally, the aforementioned extract has an ephedrine content of 0.5-1.5 mg/g and a solid content transfer rate of 18-25%.

[0011] Moreover, the extract has a content of Nodakenin ranging from 2-8 mg/g.

[0012] The preparation of the TCM extract includes the following steps: Weigh *Magnoliae Officinalis* Cortex, *Arecae Semen*, *Amomum tsaoko* Crevost & Lem., *Ephedrae Herba*, *Armeniacae Semen Amarum*, *Notopterygii Rhizoma et Radix*, *Zingiberis Rhizoma*, *Pogostemonis Herba*, *Eupatorium fortunei* Turcz., *Atractylodis Rhizoma*, *Poria cocos*, *Atractylodis Macrocephalae Rhizoma*, *Gypsum Fibrosum*, *Crataegi Fructus*, *Massa Medicata Fermentata*, *Hordei Fructus Germinatus*, *Pheretima*, *Vincetoxicum pycnostelma* Kitag., *Dryopteridis Crassirhizomatis Rhizoma*, and *Lepidium apetalum* seeds. Extract them twice with water, adding six times the amount of water for the first extraction and extracting for 1.5 hours, then adding four times the amount of water for the second extraction and extracting for 1.0 hour. Combine the extracts, filter, and concentrate the filtrate to a relative density of 1.10-1.15. Centrifuge and filter the solution, then dry the filtrate. The extract contains 1.20-1.50 mg/g of ephedrine, a solid content transfer rate of 19-22%, and 6-8 mg/g of Nodakenin.

[0013] Further, the preparation of the traditional Chinese medicine extract includes: weighing 15g of *Magnoliae Officinalis* Cortex, 9g of *Arecae Semen*, 9g of *Amomum tsaoko* Crevost & Lem., 6g of *Ephedrae Herba*, 9g of *Armeniacae Semen Amarum*, 15g of *Notopterygii Rhizoma et Radix*, 15g of *Zingiberis Rhizoma*, 15g of *Pogostemonis Herba*, 9g of *Eupatorium fortunei* Turcz., 15g of *Atractylodis Rhizoma*,

45g of *Poria cocos*, 30g of *Atractylodis Macrocephalae Rhizoma*, 15g of *Gypsum Fibrosum*, 9g of *Crataegi Fructus*, 9g of *Massa Medicata Fermentata*, 9g of *Hordei Fructus Germinatus*, 15g of *Pheretima*, 15g of *Vincetoxicum pycnostelma* Kitag., 9g of *Dryopteridis Crassirhizomatis Rhizoma*, and 15g of *Lepidium apetalum* seeds; Extract them twice with water, adding six times the amount of water for the first extraction and extracting for 1.5 hours, then adding four times the amount of water for the second extraction and extracting for 1.0 hour. Combine the extracts, filter, and concentrate the filtrate to a relative density of 1.10-1.15. Centrifuge and filter the solution, then dry the filtrate.

[0014] Further, the fingerprint chromatogram of the *Magnoliae Officinalis Cortex* extract must show a similarity of no less than 0.90 when compared to the reference fingerprint chromatogram, where the reference chromatogram contains common peaks such as *Magnolol* and *Honokiol*. The reference fingerprint chromatogram may, for example, be shown as Figure 1.

[0015] Further, the fingerprint chromatogram of *Arecae Semen* extract must show a similarity of no less than 0.90 when compared to the reference fingerprint chromatogram, where the reference chromatogram contains common peaks such as *Arecoline* and *Arecaidine*. The reference fingerprint chromatogram may, for example, be shown as Figure 2.

[0016] Further, the fingerprint chromatogram of *Amomum tsaoko* Crevost & Lem. extract must show a similarity of no less than 0.90 when compared to the reference fingerprint chromatogram, where the reference chromatogram contains the common peak of *Protocatechuic Acid*. The reference fingerprint chromatogram may,

for example, be shown as Figure 3.

[0017] A method for preparing a traditional Chinese medicine extract is characterized by weighing *Magnoliae Officinalis Cortex*, *Arecae Semen*, *Amomum tsaoko* Crevost & Lem., *Ephedrae Herba*, *Armeniacae Semen Amarum*, *Notopterygii Rhizoma et Radix*, *Zingiberis Rhizoma*, *Pogostemonis Herba*, *Eupatorium fortunei* Turcz., *Atractylodis Rhizoma*, *Poria cocos*, *Atractylodis Macrocephalae Rhizoma*, *Gypsum Fibrosum*, *Crataegi Fructus*, *Massa Medicata Fermentata*, *Hordei Fructus Germinatus*, *Pheretima*, *Vincetoxicum pycnostelma* Kitag., *Dryopteridis Crassirhizomatis Rhizoma*, and *Lepidium apetalum* seeds. Extract them twice with water, adding six times the amount of water for the first extraction and extracting for 1.5 hours, then adding four times the amount of water for the second extraction and extracting for 1.0 hour. Combine the extracts, filter, and concentrate the filtrate to a relative density of 1.10-1.15. Centrifuge and filter the solution, then dry the filtrate. The extract contains 1.20-1.50 mg/g of ephedrine, a solid content transfer rate of 19-22%, and 6-8 mg/g of Nodakenin. The fingerprint chromatogram of *Magnoliae Officinalis Cortex*, *Arecae Semen*, or *Amomum tsaoko* Crevost & Lem. is as previously defined. The present invention also relates to the application of the traditional Chinese medicine extract prepared as described above in the preparation of medications for treating Influenza H1N1, FM1, or Respiratory Syncytial Virus (RSV).

[0018] Further, the aforementioned extract is made from the following ingredients: *Magnoliae Officinalis Cortex* 50 parts, *Arecae Semen* 30 parts, *Amomum tsaoko* Crevost & Lem. 30 parts, *Ephedrae Herba* 20 parts, *Armeniacae Semen*

Amarum 30 parts, Notopterygii Rhizoma et Radix 50 parts, Zingiberis Rhizoma 50 parts, Pogostemonis Herba 50 parts, Eupatorium fortunei Turcz. 30 parts, Atractylodis Rhizoma 50 parts, Poria cocos 150 parts, Atractylodis Macrocephalae Rhizoma 100 parts, Gypsum Fibrosum 50 parts, Crataegi Fructus 30 parts, Massa Medicata Fermentata 30 parts, Hordei Fructus Germinatus 30 parts, Pheretima 50 parts, Vincetoxicum pycnostelma Kitag. 50 parts, Dryopteridis Crassirhizomatis Rhizoma 30 parts, and Lepidium apetalum seeds 50 parts.

[0019] The invention also relates to a drug made by combining the traditional Chinese medicine extract described above with pharmaceutically acceptable excipients or additives.

[0020] Specifically, the drug is selected from decoctions, granules, capsules, tablets, oral solutions, pills, soft capsules, drops, tinctures, syrups, suppositories, gels, sprays, or injectables.

[0021] Further, the drug is in the form of granules, and the excipients or additives are preferably dextrin and sucralose.

[0022] Further, the drug may also include antiviral agents for upper respiratory tract infections, such as Ribavirin and/or Oseltamivir Phosphate.

[0023] The present invention also provides a method for detecting the fingerprint chromatogram of a Chinese medicinal extract or drug as described above. The method is characterized in that a sample solution is subjected to HPLC analysis, where the chromatographic conditions for HPLC include: the use of a C18 chromatographic column, methanol as mobile phase A, and a 0.1% aqueous phosphoric acid solution as mobile phase B. The elution in the HPLC detection

follows a gradient elution program as follows: 0~5 min, 0% A; 5~25 min, 0%~15% A; 25~60 min, 15%~55% A; 60~75 min, 55%~100% A; 75~80 min, 100% A.

[0024] The sample solution is prepared from a Traditional Chinese Medicine extract or drug for testing purposes. The preparation method, for example, can involve taking 1g of granules, placing it in a conical flask with a stopper, adding 25mL of water, and sonicating for 30 minutes to obtain the solution.

[0025] Further, the chromatographic conditions include: a flow rate of 1.0 mL/min, a column temperature of 30°C, and a detection wavelength of 250 nm.

[0026] Furthermore, the fingerprint chromatogram is shown in Figure 14.

[0027] Specifically, the characteristic chromatogram of the sample should show 10 characteristic peaks, with the corresponding peak for the reference peak being peak S. The relative retention time of each characteristic peak to peak S should be within $\pm 10\%$ of the specified value, preferably within 5%. The specified relative retention times are as follows: 0.11 (Peak 1), 0.27 (Peak 2), 0.36 (Peak 3), 0.38 (Peak 4), 0.41 (Peak 5), 0.84 (Peak 6), 0.92 (Peak 7), 1.00 [Peak 8 (S)], 1.19 (Peak 9), 1.29 (Peak 10).

[0028] The present invention has developed a new Chinese medicine composition, which improves the quality standards of the composition. Furthermore, by using influenza virus H1N1/FM1 strain infection models and respiratory syncytial virus infection models, the effectiveness of the composition in treating viral upper respiratory tract infections has been evaluated. The results show that the composition can reduce the viral load and inflammatory cytokines in lung tissues, indicating its enhanced therapeutic effect against specific common viral infections, providing a

basis for further clinical research.

BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWINGS

- [0029] • Figure 1: Fingerprint chromatogram of *Magnolia officinalis* material;
Peak 6: Honokiol; Peak 7 (S): Magnolol.
- [0030] • Figure 2: Fingerprint chromatogram of *Arecae Semen Tostum* material;
Peak 1: Arecoline; Peak 3 (S): Arecaidine.
- [0031] • Figure 3: Fingerprint chromatogram of *Amomum tsaoko* Crevost &
Lem. material; Peak 1: Protocatechuic acid.
- [0032] • Figure 4: Full wavelength scan 3D chromatogram of the sample
solution.
- [0033] • Figure 5: Chromatogram for wavelength investigation of the sample
solution.
- [0034] • Figure 6: Chromatogram for mobile phase ratio investigation.
- [0035] • Figure 7: Chromatogram for sample preparation method investigation.
- [0036] • Figure 8: Durability investigation chromatogram.
- [0037] • Figure 9: Precision investigation chromatogram.
- [0038] • Figure 10: Reproducibility investigation chromatogram.
- [0039] • Figure 11: Stability investigation chromatogram.
- [0040] • Figure 12: Overlay chromatogram of 20 batches of formulations.
- [0041] • Figure 13: Reference fingerprint chromatogram.
- [0042] • Figure 14: Reference fingerprint chromatogram and identification
results of each characteristic peak; where 1 - Adenine, 2 - Uridine, 3 - Guanosine, 4 -

Inosine, 5 - 5-Hydroxymethylfurfural, 6 - Magnoloside A, 7 - Bergaptol-O-glucopyranoside, 8 - Nodakenin, 9 - 6'-O-trans-Feruloylnodakenin, 10 - Hydroxyphenethylanisate.

DETAILED DESCRIPTION OF EMBODIMENTS

[0043] Oseltamivir is a neuraminidase inhibitor used for the treatment of influenza A and B viruses. Ribavirin is a broad-spectrum antiviral agent, clinically used for treating respiratory syncytial virus, influenza A, and B, though it is not highly recommended by the FDA. This invention aims to provide a Chinese medicine composition, its preparation method, and its application. The following description will provide specific details based on commonly used drugs for influenza or respiratory syncytial virus, incorporating experimental content.

[0044] It should be particularly noted that similar substitutions and modifications made to the present invention are obvious to those skilled in the art and are considered to be included in the scope of the invention. The relevant personnel can clearly make modifications, appropriate changes, and combinations to the methods and applications described herein without deviating from the content, spirit, and scope of the present invention in order to implement and apply the technology of the invention. It is evident that the described examples are merely part of the embodiments of the invention and not all of the embodiments.

[0045] Unless otherwise specified, the invention should be carried out under conventional conditions or the conditions recommended by the manufacturer. Raw materials, excipients, reagents, or instruments used, unless the manufacturer is

specified, should be considered as standard products available commercially.

[0046] Experiment Example 1: Preparation Process Investigation

[0047] 1. Extraction Solvent Investigation

[0048] Weigh 15g of *Magnoliae Officinalis Cortex*, 9g of *Arecae Semen*, 9g of *Amomum tsaoko* Crevost & Lem., 6g of *Ephedrae Herba*, 9g of *Armeniacae Semen Amarum*, 15g of *Notopterygii Rhizoma et Radix*, 15g of *Zingiberis Rhizoma*, 15g of *Pogostemonis Herba*, 9g of *Eupatorium fortunei Turcz.*, 15g of *Atractylodis Rhizoma*, 45g of *Poria cocos*, 30g of *Atractylodis Macrocephalae Rhizoma*, 15g of *Gypsum Fibrosum*, 9g of *Crataegi Fructus*, 9g of *Massa Medicata Fermentata*, 9g of *Hordei Fructus Germinatus*, 15g of *Pheretima*, 15g of *Vincetoxicum pycnostelma* Kitag., 9g of *Dryopteridis Crassirhizomatis Rhizoma*, and 15g of *Lepidium apetalum* seeds; Extract them twice with water, first extracting for 1.5 hours and then for 1.0 hour. Combine the extracts, filter, and concentrate the filtrate to a relative density of 1.10~1.15. Centrifuge, filter, and vacuum dry the filtrate, then spray-dry and pulverize to obtain the intermediate composition. The transfer rate of ephedrine, as well as the solid content transfer rate with different solvent volumes, are as follows:

Solvent Volume Ratio	Ephedrine & Pseudoephedrine Transfer Rate (%)	Solid Content Transfer Rate (%)
4,3	48.17	15.43
6,4	61.17	19.71
8,6	61.96	21.05
10,8	55.81	22.52

[0049] Calculation Formula:

[0050] Transfer Rate of Ephedrine(%)=total amount of ephedrine in the extract/total amount of ephedrine in the raw material*100%

[0051] Solid Content Transfer Rate(%)=Total amount of dry extract in the extract / Amount of medicinal material input

[0052] The total transfer rate refers to the ratio of the total amount of ephedrine hydrochloride and pseudoephedrine hydrochloride in the extract to the amount of ephedrine hydrochloride and pseudoephedrine hydrochloride in the raw material.

[0053] The experimental results show that the transfer rates of ephedrine hydrochloride and pseudoephedrine hydrochloride, as well as the solid content transfer rate, increase with the increase in water volume. When the solvent volume ratio increases from 4, 3 to 6, 4, the transfer rates of all indicators show a more significant increase. However, as the water volume continues to increase, the growth trend becomes more gradual, and the transfer rate decreases when the solvent volume becomes excessively high. Considering both efficiency and the transfer rates of the target components, the optimal water volumes were determined as 6 times for the first extraction and 4 times for the second extraction.

[0054] 2. Soaking Time Investigation

[0055] Weigh another batch of 15g of *Magnoliae Officinalis Cortex*, 9g of *Arecae Semen*, 9g of *Amomum tsaoko* Crevost & Lem., 6g of *Ephedrae Herba*, 9g of *Armeniacae Semen Amarum*, 15g of *Notopterygii Rhizoma et Radix*, 15g of *Zingiberis Rhizoma*, 15g of *Pogostemonis Herba*, 9g of *Eupatorium fortunei* Turcz., 15g of *Atractylodis Rhizoma*, 45g of *Poria cocos*, 30g of *Atractylodis Macrocephalae Rhizoma*, 15g of *Gypsum Fibrosum*, 9g of *Crataegi Fructus*, 9g of *Massa Medicata Fermentata*, 9g of *Hordei Fructus Germinatus*, 15g of *Pheretima*, 15g of *Vincetoxicum pycnostelma* Kitag., 9g of *Dryopteridis Crassirhizomatis Rhizoma*, and

15g of *Lepidium apetalum* seeds, making 3 batches. Extract them twice with water, adding six times the amount of water for the first extraction and extracting for 1.5 hours, then adding four times the amount of water for the second extraction and extracting for 1.0 hour. The soaking times for the 3 batches were 0, 30, and 60 minutes, respectively. Combine the extracts, filter, and concentrate the filtrate to a relative density of 1.10~1.15. Centrifuge, filter, and vacuum dry the filtrate, then spray-dry and pulverize to obtain the intermediate composition.

[0056] The effects of soaking time on the transfer rates of ephedrine hydrochloride and pseudoephedrine hydrochloride, as well as the solid content transfer rate, were investigated. The experimental results are as follows:

Soaking Time (min)	Ephedrine & Pseudoephedrine Transfer Rate (%)	Solid Content Transfer Rate (%)
0	58.76	18.47
30	61.67	19.84
60	59.47	19.68

[0057] Calculation Formula:

[0058] Transfer Rate of Ephedrine(%)=total amount of ephedrine in the extract/total amount of ephedrine in the raw material*100%

[0059] Solid Content Transfer Rate(%)=Total amount of dry extract in the extract / Amount of medicinal material input

[0060] The experimental results indicate that the soaking time has little effect on the total transfer rate of ephedrine hydrochloride and pseudoephedrine hydrochloride, as well as the solid content transfer rate. Therefore, it was decided not to include a soaking step in the extraction process and to proceed directly with the extraction.

[0061] 3. Investigation of Extraction Time

[0062] For each sample, 15g of *Magnoliae Officinalis Cortex*, 9g of *Arecae Semen*, 9g of *Amomum tsaoko Crevost & Lem.*, 6g of *Ephedrae Herba*, 9g of *Armeniacae Semen Amarum*, 15g of *Notopterygii Rhizoma et Radix*, 15g of *Zingiberis Rhizoma*, 15g of *Pogostemonis Herba*, 9g of *Eupatorium fortunei Turcz.*, 15g of *Atractylodis Rhizoma*, 45g of *Poria cocos*, 30g of *Atractylodis Macrocephalae Rhizoma*, 15g of *Gypsum Fibrosum*, 9g of *Crataegi Fructus*, 9g of *Massa Medicata Fermentata*, 9g of *Hordei Fructus Germinatus*, 15g of *Pheretima*, 15g of *Vincetoxicum pycnostelma Kitag.*, 9g of *Dryopteridis Crassirhizomatis Rhizoma*, and 15g of *Lepidium apetalum* seeds were prepared into one batch, with a total of five batches. Each batch was extracted twice with water, with the first extraction using six times the amount of water and the second extraction using four times the amount. The first extraction times were 60 min, 75 min, 90 min, 105 min, and 120 min, and the second extraction times were 30 min, 45 min, 60 min, 75 min, and 90 min. The influence of extraction time on the transfer rate of ephedrine hydrochloride and pseudoephedrine hydrochloride, as well as the transfer rate of solid content, was investigated. The experimental results are as follows:

Extraction Time (min)	Ephedrine & Pseudoephedrine Transfer Rate (%)	Solid Content Transfer Rate (%)
60,30	61.41	16.49
75,45	62.04	17.73
90,60	61.61	19.46
105,75	64.32	19.61
120,90	58.63	19.97

[0063] Calculation Formula:

[0064] Transfer Rate of Ephedrine(%)=total amount of ephedrine in the

extract/total amount of ephedrine in the raw material*100%

[0065] Solid Content Transfer Rate(%)=Total amount of dry extract in the extract / Amount of medicinal material input

[0066] The experimental results show that both the ephedrine and pseudoephedrine transfer rates and solid content transfer rates increase as extraction time extends. When the extraction time increased from 60, 30 minutes to 90, 60 minutes, the increase in these parameters was more significant. As the extraction time continued to increase, the growth rate of the parameters gradually slowed. Therefore, the optimal extraction time is determined as 90 minutes for the first extraction and 60 minutes for the second extraction.

[0067] 4. Extraction Process Verification

[0068] To verify the selected extraction process, scaling-up verification experiments were conducted based on the results of the single-factor experiments. In previous experiments, several main components of the extract showed significant fluctuations, which affected the therapeutic efficacy. Therefore, control of the entire process, from raw materials to preparation methods, was strengthened to achieve effective and controllable extracts. 15g of *Magnoliae Officinalis Cortex*, 9g of *Arecae Semen*, 9g of *Amomum tsaoko Crevost & Lem.*, 6g of *Ephedrae Herba*, 9g of *Armeniacae Semen Amarum*, 15g of *Notopterygii Rhizoma et Radix*, 15g of *Zingiberis Rhizoma*, 15g of *Pogostemonis Herba*, 9g of *Eupatorium fortunei Turcz.*, 15g of *Atractylodis Rhizoma*, 45g of *Poria cocos*, 30g of *Atractylodis Macrocephalae Rhizoma*, 15g of *Gypsum Fibrosum*, 9g of *Crataegi Fructus*, 9g of *Massa Medicata Fermentata*, 9g of *Hordei Fructus Germinatus*, 15g of *Pheretima*, 15g of

Vincetoxicum pycnostelma Kitag., 9g of *Dryopteridis Crassirhizomatis Rhizoma*, and 15g of *Lepidium apetalum* seeds were used for one batch, and a total of 12 batches were prepared (with unique fingerprint chromatogram control standards established for important herbs such as *Magnolia officinalis*, *Arecae Semen Tostum*, and *Amomum tsaoko* Crevost & Lem., and the medicinal materials complied with the latest pharmacopoeia standards). The batches were extracted twice with water, with the first extraction using six times the amount of water for 1.5 hours, and the second extraction using four times the amount of water for 1.0 hour. Every four batches were combined into one group, resulting in three groups in total. The transfer rates of ephedrine hydrochloride and pseudoephedrine hydrochloride, solid content transfer rates, and other important indicators were measured to assess the stability and feasibility of the process. The experimental results are as follows:

Group	Total Transfer Rate of Ephedrine & Pseudoephedrine (%)	Solid Content Transfer Rate (%)	Ephedrine (mg/g)	Nodakenin (mg/g)
1	62.42	19.11	1.29	6.02
2	59.67	20.95	1.33	6.44
3	60.03	20.61	1.42	7.77

[0069] The verification results showed that the selected process was stable, feasible, and reproducible. Therefore, the optimal extraction process was determined to be the following: two extractions with water, the first extraction using six times the amount of water for 1.5 hours, and the second extraction using four times the amount of water for 1.0 hour.

[0070] 5. Fingerprint Chromatogram Control Standards for *Magnolia officinalis*,

Arecae Semen Tostum, and Amomum tsaoko Crevost & Lem.

[0071] 5.1 Fingerprint Chromatogram Control Standards for *Magnolia officinalis* and its Decoction Pieces

[0072] Chromatographic conditions and system suitability test: Use C18 chromatography column (Waters CORTECTS C18, 150mm×4.6mm, 2.7μm) with octadecylsilane-bonded silica as the stationary phase. Acetonitrile is used as mobile phase A, and 0.1% acetic acid solution as mobile phase B, performing gradient elution according to the table below. The column temperature is set at 35°C, with a flow rate of 0.8 mL/min and detection wavelength at 230 nm. The theoretical plate number based on the Magnolol peak should not be less than 4000.

Time (min)	Acetonitrile A (%)	0.1% Acetic acid B (%)
0~13	10→15	90→85
13~38	15→75	85→25
38~40	75→95	25→5
40~45	95	5

[0073] Preparation of Reference Solution: Weigh an appropriate amount of Magnolol and Honokiol reference substance precisely, and add methanol to prepare a mixed solution containing 200 μg per 1 ml, which is the reference solution.

[0074] Preparation of Test Solution: Weigh precisely 1 g of the powdered drug (sieved through a No. 3 sieve), place it into a conical flask with a stopper, and add precisely 25 ml of 50% methanol solution. Shake well, seal tightly, and let it soak for 24 hours. Filter the mixture and collect the filtrate to obtain the test solution.

[0075] Determination Method: Accurately pipette 10 μl of the reference solution and 10 μl of the test solution, and inject each into the liquid chromatograph for

analysis.

[0076] The test solution's chromatographic fingerprint should present a chromatographic peak with the same retention time as that in the chromatographic peak profile of the reference solution (Figure 1). According to the TCM chromatographic fingerprint similarity evaluation system, the similarity of the test fingerprint and the reference fingerprint should not be less than 0.90.

[0077] 5.2 Control Standard for Fingerprint Chromatogram of Arecae Semen Tostum and Decoction Pieces

[0078] Chromatographic Conditions and System Suitability Test: Use strong cation exchange bonded silica gel as the stationary phase (Thermo BioBasic SCX column, 25 cm long, 4.6 mm internal diameter, 5 μ m particle size). The mobile phase consists of acetonitrile-0.2% phosphoric acid solution (adjust pH to 3.8 with ammonia water) in a 65:35 ratio. Set the column temperature to 35°C, with a flow rate of 1.2 ml/min and a detection wavelength of 210 nm. The theoretical plate count, calculated based on arecoline, should be no less than 10,000.

[0079] Preparation of Reference Solution: Weigh an appropriate amount of arecoline hydrobromide reference substance precisely, and add methanol to prepare a solution containing 50 μ g per 1 ml.

[0080] Preparation of Test Solution: Weigh precisely 0.5 g of the powdered drug (sieved through a No. 2 sieve), place it into a conical flask with a stopper, and add precisely 50 ml of 50% methanol solution. Treat the solution with ultrasound for 30 minutes, cool it, shake well, and filter. Collect the filtrate to obtain the test solution.

[0081] Determination Method: Accurately pipette 10 μ l of both the reference

solution and the test solution and inject them into the liquid chromatograph for analysis. Record the chromatogram.

[0082] The test solution's chromatographic fingerprint should present a chromatographic peak with the same retention time as that in the chromatographic peak profile of the reference solution (Figure 2). According to the TCM chromatographic fingerprint similarity evaluation system, the similarity of the test fingerprint and the reference fingerprint should not be less than 0.90.

[0083] 5.3 Control Standard for Fingerprint Chromatogram of *Amomum tsaoko* Crevost & Lem. and Decoction Pieces

[0084] Chromatographic Conditions and System Suitability Test: Use octadecylsilane-bonded silica gel as the stationary phase (Waters CORTECS T3 column, 15 cm long, 4.6 mm internal diameter, 2.7 μm particle size). The mobile phase consists of acetonitrile (A) and 0.1% formic acid solution (B), with gradient elution as follows. Set the column temperature to 30°C, with a flow rate of 0.8 ml/min and a detection wavelength of 254 nm. The theoretical plate count, calculated based on gallic acid peak, should be no less than 10,000.

Time (min)	Mobile Phase A (%)	Mobile Phase B (%)
0~25	0→25	100→75
25~35	25→50	75→50
35~40	50→95	50→5
40~45	95	5

[0085] Preparation of Reference Solution: Weigh an appropriate amount of protocatechuic acid reference substance precisely, and add methanol to prepare a solution containing 200 μg per 1 ml.

[0086] Preparation of Test Solution: Weigh precisely 1 g of the powdered drug (sieved through a No. 2 sieve), add precisely 25 ml of 50% methanol solution. Treat the mixture with ultrasound for 30 minutes, cool it, shake well, and filter. Collect the filtrate to obtain the test solution.

[0087] Determination Method: Accurately pipette 5–10 μ l of the reference solution and 10 μ l of the test solution and inject them into the liquid chromatograph for analysis. Record the chromatogram.

[0088] The test solution's chromatographic fingerprint should present a chromatographic peak with the same retention time as that in the chromatographic peak profile of the reference solution (Figure 3). According to the TCM chromatographic fingerprint similarity evaluation system, the similarity of the test fingerprint and the reference fingerprint should not be less than 0.90.

[0089] Example 2: Preparation of the Formulation

[0090] Preparation Example 1: Traditional Chinese Medicine Compound Granules

[0091] Formula: *Magnoliae Officinalis Cortex* 50 parts, *Arecae Semen* 30 parts, *Amomum tsaoko* Crevost & Lem. 30 parts, *Ephedrae Herba* 20 parts, *Armeniacae Semen Amarum* 30 parts, *Notopterygii Rhizoma et Radix* 50 parts, *Zingiberis Rhizoma* 50 parts, *Pogostemonis Herba* 50 parts, *Eupatorium fortunei* Turcz. 30 parts, *Atractylodis Rhizoma* 50 parts, *Poria cocos* 150 parts, *Atractylodis Macrocephalae Rhizoma* 100 parts, *Gypsum Fibrosum* 50 parts, *Crataegi Fructus* 30 parts, *Massa Medicata Fermentata* 30 parts, *Hordei Fructus Germinatus* 30 parts, *Pheretima* 50 parts, *Vincetoxicum pycnostelma* Kitag. 50 parts, *Dryopteridis Crassirhizomatis*

Rhizoma 30 parts, and *Lepidium apetalum* seeds 50 parts.

[0092] Preparation Method for the Granules:

[0093] Add the above herbal materials to water for reflux extraction twice. For the first extraction, use 6 times the weight of water and extract for 1.5 hours. For the second extraction, use 4 times the weight of water and extract for 1.0 hour. Combine the extract liquids, filter them, and concentrate the filtrate to a relative density of 1.10–1.15. Centrifuge and filter the liquid, then perform vacuum drying. Spray-dry the mixture and pulverize to obtain the intermediate composition. Add sucralose and dextrin, mix thoroughly, and form granules.

[0094] Preparation Example 2: Traditional Chinese Medicine Compound Capsules

[0095] Formula: *Magnoliae Officinalis* Cortex 50 parts, *Arecae Semen* 30 parts, *Amomum tsaoko* Crevost & Lem. 30 parts, *Ephedrae Herba* 20 parts, *Armeniacae Semen Amarum* 30 parts, *Notopterygii Rhizoma et Radix* 50 parts, *Zingiberis Rhizoma* 50 parts, *Pogostemonis Herba* 50 parts, *Eupatorium fortunei* Turcz. 30 parts, *Atractylodis Rhizoma* 50 parts, *Poria cocos* 150 parts, *Atractylodis Macrocephalae Rhizoma* 100 parts, *Gypsum Fibrosum* 50 parts, *Crataegi Fructus* 30 parts, *Massa Medicata Fermentata* 30 parts, *Hordei Fructus Germinatus* 30 parts, *Pheretima* 50 parts, *Vincetoxicum pycnostelma* Kitag. 50 parts, *Dryopteridis Crassirhizomatis Rhizoma* 30 parts, and *Lepidium apetalum* seeds 50 parts.

[0096] Preparation Method for the Capsules:

[0097] Add the herbal materials to water for reflux extraction twice. For the first extraction, use 6 times the weight of water and extract for 1.5 hours. For the second

extraction, use 4 times the weight of water and extract for 1.0 hour. Combine the extract liquids, filter them, and concentrate the filtrate to a relative density of 1.10–1.15. Centrifuge and filter the liquid, then perform vacuum drying. Spray-dry the mixture, granulate it, and encapsulate to prepare the capsules.

[0098] Preparation Example 3: Traditional Chinese Medicine Compound Tablets

[0099] Formula: *Magnoliae Officinalis Cortex* 50 parts, *Arecae Semen* 30 parts, *Amomum tsaoko* Crevost & Lem. 30 parts, *Ephedrae Herba* 20 parts, *Armeniacae Semen Amarum* 30 parts, *Notopterygii Rhizoma et Radix* 50 parts, *Zingiberis Rhizoma* 50 parts, *Pogostemonis Herba* 50 parts, *Eupatorium fortunei* Turcz. 30 parts, *Atractylodis Rhizoma* 50 parts, *Poria cocos* 150 parts, *Atractylodis Macrocephalae Rhizoma* 100 parts, *Gypsum Fibrosum* 50 parts, *Crataegi Fructus* 30 parts, *Massa Medicata Fermentata* 30 parts, *Hordei Fructus Germinatus* 30 parts, *Pheretima* 50 parts, *Vincetoxicum pycnostelma* Kitag. 50 parts, *Dryopteridis Crassirhizomatis Rhizoma* 30 parts, and *Lepidium apetalum* seeds 50 parts.

[00100] Preparation Method for the Tablets:

[00101] Add the herbal materials to water for reflux extraction twice. For the first extraction, use 6 times the weight of water and extract for 1.5 hours. For the second extraction, use 4 times the weight of water and extract for 1.0 hour. Combine the extract liquids, filter them, and concentrate the filtrate to a relative density of 1.10–1.15. Centrifuge and filter the liquid, then perform vacuum drying. Spray-dry the mixture to obtain the extract powder, then add microcrystalline cellulose and other excipients, and compress into tablets.

[00102] Experimental Example 3: Therapeutic Effect of the Composition

Granules of the Present Invention on Influenza Virus H1N1/FM1 Strain Infection

[00103] Experimental Materials

[00104] 1.1 Test Drug: Granules prepared according to Preparation Example 1, provided by Jiangsu Kangyuan Pharmaceutical Co., Ltd.

[00105] 1.2 Positive Control Drugs

[00106] 1.2.1 Oseltamivir Phosphate Granules (Kewei): Manufactured by Yichang Dongyangguang Changjiang Pharmaceutical Co., Ltd., Composition: Each packet of granules contains 15 mg of Oseltamivir Phosphate.

[00107] 1.2.2 Ribavirin Granules: Manufactured by Sichuan Baili Pharmaceutical Co., Ltd., Composition: The main ingredient is Ribavirin. Specification: 50 mg.

[00108] 1.3 Reagents

Reagent Name	Batch Number	Manufacturer	Reagent Use
Isoflurane	S200106	Shanghai Yuyan Scientific Instrument Co., Ltd.	Mice Anesthesia
Xylene	20170705	China National Pharmaceutical Group Chemical Reagents Co., Ltd.	Lung Tissue Pathology
Hematoxylin Staining Solution	DH0001/04 05A17	Beijing Boruijie Technology Co., Ltd.	Lung Tissue Pathology
Eosin (Eosin Y)	20150915	Beijing Chemical Factory	Lung Tissue Pathology
Formaldehyde	F20180825	China National Pharmaceutical Group Chemical Reagents Co., Ltd.	Lung Tissue Pathology
95% Ethanol	20180208	Beijing Chemical Factory	Lung Tissue Pathology
Anhydrous Ethanol	20180208	Beijing Chemical Factory	Lung Tissue Pathology
Neutral Resin	20170815	Shanghai Specimen Model Factory	Lung Tissue Pathology

[00109] 1.4 Instruments

Instrument Name	Model	Manufacturer	Instrument Use
A2 Type Biological Safety Cabinet	MSC-Advantage 1.8	Thermo Fisher Scientific, USA	Animal Infection, Dissection
Electronic Balance	YP1002 MAX100g	Shanghai Yueping Scientific Instrument Co., Ltd.	Weighing Mice Body Weight
Electronic Analytical Balance	AR1140 MAX110g	Ohaus Corporation, USA	Weighing Drugs, Reagents
Electronic Balance	AL204 MAX210g	Mettler Toledo Instrument Co., Ltd.	Weighing Tissue Weight
IVC Mice Cage	ZJ-4	Suzhou Feng's Co., Ltd.	Mice Breeding
Low-Speed High-Capacity Centrifuge	Eppendorf-5810R	Eppendorf, Germany	Centrifugation of Lung Tissue
Tissue Homogenizer	FastPre-24TM	MP Biomedicals, USA	Processing Tissue Samples
Automatic Dehydrator	TP 1020	Leica Microsystems, Germany	Lung Tissue Pathology
Paraffin Embedding Machine	EG 1140H	Leica Microsystems, Germany	Lung Tissue Pathology
Fully Automatic Rotary Microtome	HM 355S	Microm, Germany	Lung Tissue Pathology
Automatic Staining Machine	XL 5010	Autostainer, Germany	Lung Tissue Pathology
Digital Photomicrograph Biological Microscope	DM 2500	Leica Microsystems, Germany	Lung Tissue Pathology
Automatic Optical Photomicrograph Biological Microscope	DMLB-HC	Leica Microsystems, Germany	Lung Tissue Pathology

[00110] 1.5 Experimental Animals

Species	Grade	Weight	Quantity	Gender	Certificate No.	Animal License
ICR Mice	SPF Grade	13-15 g	70	Half Male, Half Female	1100112111110362982	SCXK(Jing)2021-0006

Source: Beijing Weitong Lihua Experimental Animal Technology Co., Ltd.

Breeding Conditions: ABSL-2 Laboratory, -20Pa, Temperature 22±1°C, Humidity 40~50%
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[00111] 1.6 Virus Strain

[00112] The H1N1 Influenza Virus FM1 strain was purchased from the American Type Culture Collection (ATCC). It was regularly passaged in our ABSL-2 laboratory and stored at -80°C for future use.

[00113] Dosage Design and Drug Preparation

[00114] 2.1 Preparation Example 1:

[00115] Drug Solution Preparation: Before the experiment, granules were dissolved in distilled water and prepared to a final concentration of 26.4g of crude drug/kg/d. Administration was performed by oral gavage at a dose of 0.2 mL/10 g body weight/administration, once per day for 4 consecutive days.

[00116] 2.2 Oseltamivir Phosphate: The dosage for mice was 27.5 mg/kg/d, equivalent to the human clinical dose. Administration was performed by oral gavage at a dose of 0.2 mL/10 g body weight/administration, once per day for 4 consecutive days.

[00117] 2.3 Ribavirin: The dosage for mice was 82.5 mg/kg/d. Administration was performed by oral gavage at a dose of 0.2 mL/10 g body weight/administration, once per day for 4 consecutive days.

[00118] 2.4 Combination Group 1: Preparation Example 1 13.2g of crude drug/kg/d + Oseltamivir Phosphate 13.7 mg/kg/d. Administration method as above.

[00119] 2.5 Combination Group 2: Preparation Example 1 13.2g of crude drug/kg/d + Ribavirin 41.2 mg/kg/d. Administration method as above.

[00120] 3. Experimental Methods

[00121] Seventy ICR mice, weighing 14 ± 1 g, with equal numbers of males and females, were randomly divided into seven groups based on body weight: normal control group, model control group, oseltamivir phosphate group, ribavirin group, composition group, oseltamivir phosphate + composition group, ribavirin + composition group. Except for the normal control group, the mice were lightly anesthetized with isoflurane and infected intranasally with 15 LD₅₀ of influenza virus (H1N1/FM1 strain), 35 μ L per mouse. Treatment was initiated on the day of infection, with oral gavage administered at 0.2 mL/10 g body weight once daily for 4 consecutive days. The normal control group and model control group received distilled water via gavage under the same conditions. On day 5, body weights were measured for all groups, and the lungs were dissected and weighed. Lung tissue was subjected to hematoxylin and eosin (HE) staining for pathological examination. Lung index and lung index inhibition rate were calculated.

$$[00122] \text{ Lung Index (\%)} = \text{Lung wet weight (g)} / \text{Body weight (g)} \times 100$$

$$[00123] \text{ Lung Index Inhibition Rate (\%)} = (\text{Lung weight of model control group (g)} - \text{Lung weight of treatment group (g)}) / (\text{Lung weight of model control group (g)} - \text{Lung weight of normal control group (g)}) \times 100$$

[00124] Microscopic Standard:

[00125] "–": No exudation or congestion observed in the lung interstitium, no enlargement of interstitial cells, no inflammation around small bronchi, and the tissue structure is normal.

[00126] "+": No significant exudative inflammation in lung tissue or alveolar interstitium, no large areas of congestion, but a small amount of localized

inflammation around the small bronchi, mainly lymphocytic.

[00127] "++": No widespread inflammatory or mucous exudation in lung tissue or alveolar interstitium, with localized small patches of mucous exudation. There is localized inflammation around small bronchi, mainly lymphocytic, and localized proliferation of epithelial cells (segmental).

[00128] "+++": Widespread inflammatory and mucous exudation in lung tissue and alveolar interstitium, with inflammation predominantly composed of lymphocytes, a small amount of neutrophils and eosinophils, with uneven cell size and clustering. There is significant perivascular inflammation, localized inflammation around small bronchi, and epithelial cell hyperplasia, with severe perivascular inflammation.

[00129] Statistical Methods: The results were analyzed statistically using inter-group comparison with a t-test.

[00130] 4. Effects of the Composition Granules on Lung Index and Lung Index Inhibition Rate

[00131] Research results (Table 1) show that after infection of mice with H1N1/FM1 influenza virus, the lung index of the model control group was significantly higher compared to the normal control group, with a significant difference ($P < 0.01$). After treatment with the composition granules for 4 days starting on the day of infection, the lung indices of the oseltamivir phosphate group, composition group, oseltamivir phosphate + composition group, and ribavirin + composition group were significantly lower compared to the model control group, indicating that the composition has a synergistic effect with antiviral drugs used for

upper respiratory tract infections, significantly enhancing the efficacy against influenza virus.

[00132] Table 1: Effects of Composition Granules on the Lung Index of Mice Infected with H1N1/FM1 Influenza Virus

Group	Dose	Number of Animals	Lung Index (%)	Inhibition Rate (%)
Normal Control Group	-	10	0.75±0.03	
Model Control Group	-	10	1.01±0.03 ^{##}	
Oseltamivir Phosphate Group	27.5 mg/kg/d	10	0.88±0.06 ^{**}	0.74
Ribavirin Group	82.5 mg/kg/d	10	0.96±0.08	0.41
Composition Group	26.4g crude drug/kg /d	10	0.95±0.07 [*]	0.46
Oseltamivir Phosphate + Composition Group	13.7 mg/kg/d+13.2g crude drug/kg /d	10	0.87±0.06 ^{**}	0.82
Ribavirin + Composition Group	41.2 mg/kg/d+13.2g crude drug/kg /d	10	0.89±0.07 ^{**}	0.75

[00133] Note: Compared with the normal control group, ^{##}P<0.01; compared with the model control group, ^{**}P<0.01, ^{*}P<0.05.

[00134] Experimental Example 4: Therapeutic Effect of the Composition Granules on Respiratory Syncytial Virus Infection

[00135] Materials

[00136] 1.1 Test Drug: Granules prepared according to Example 1, provided by Jiangsu Kangyuan Pharmaceutical Co., Ltd.

[00137] 1.2 Positive Control Drugs

[00138] 1.2.1 Oseltamivir Phosphate Granules (Colvax): Produced by Yichang

Dongyangguang Changjiang Pharmaceutical Co., Ltd. Components: Each packet of granules contains 15 mg of Oseltamivir Phosphate.

[00139] 1.2.2 Ribavirin Granules: Produced by Sichuan Baile Pharmaceutical Co., Ltd. Components: The main ingredient of this product is Ribavirin. Specifications: 50 mg.

[00140] 1.3 Reagents

Reagent Name	Lot Number	Manufacturer	Purpose
Isoflurane	S200106	Shanghai Yuyan Scientific Instrument Co., Ltd.	Mouse anesthesia
IL-4	239645-001	Thermo Fisher	Lung tissue factor detection
IL-33	230852-006	Thermo Fisher	Lung tissue factor detection

[00141] 1.4 Instruments

Instrument Name	Model	Manufacturer	Purpose
A2 Biological Safety Cabinet	MSC-Advantage 1.8	Thermo Fisher, USA	Animal infection, dissection
Electronic Balance	YP1002 MAX100g	Shanghai Yueping Scientific Instrument Co., Ltd.	Weighing mouse body weight
Electronic Analytical Balance	AR1140 MAX110g	Ohaus, USA	Weighing drugs, reagents
Electronic Balance	AL204 MAX210g	Mettler-Toledo Instruments, Switzerland	Weighing tissue weight
IVC Mouse Breeding Cage	ZJ-4	Suzhou Fengshi Co., Ltd.	Breeding mice
Low Temperature High-Speed Centrifuge	Eppendorf-5810R	Eppendorf, Germany	Centrifugation of lung tissue
Tissue Homogenizer	FastPre-24TM	MP, USA	Processing tissue samples

[00142] 1.5 Experimental Animals

Species	Level	Body Weight	Quantity	Gender	Certification Number	Animal License
BALB/C Mice	SPF level:	13-15 g	70	half male and half female	110011211111036318 5 110011211111036306 8	SCXK(Jing)2021-0006
Source: Provided by Beijing Weitong Lihua Experimental Animal Technology Co., Ltd.						
Breeding Conditions: ABSL-2 laboratory, -20Pa, temperature $22 \pm 1^{\circ}$ C, humidity 40~50%						

[00143] 1.6 Virus Strain

[00144] Respiratory Syncytial Virus (RSV) strain purchased from the American Type Culture Collection (ATCC). Passaged routinely in the laboratory's ABSL-2 facility and stored at -80° C for future use.

[00145] Dose Design and Drug Preparation

[00146] 2.1 Preparation Example 1:

[00147] Drug Solution Preparation: Take the granules, add distilled water, and dilute to a final volume of 40 mL. The dosage is 26.4 g crude drug/kg/day. Administer by gavage at a dosage of 0.2 mL/10 g body weight per dose, once daily, for 4 consecutive days.

[00148] 2.2 Oseltamivir Phosphate Granules: For mice, the dose is 27.5 mg/kg/day, which is equivalent to the clinical human dose. Administer by gavage at a dosage of 0.2 mL/10 g body weight per dose, once daily, for 4 consecutive days.

[00149] 2.3 Ribavirin Granules: For mice, the dose is 82.5 mg/kg/day. Administer by gavage at a dosage of 0.2 mL/10 g body weight per dose, once daily, for 4 consecutive days.

[00150] 2.4 Composition Group 1:

[00151] Granules prepared according to Example 1, 13.2 g crude drug/kg/day + Oseltamivir Phosphate 13.7 mg/kg/day. Administer by the same method as described above.

[00152] 2.5 Composition Group 2:

[00153] Granules prepared according to Example 1, 13.2 g crude drug/kg/day + Ribavirin 41.2 mg/kg/day. Administer by the same method as described above.

[00154] 3 Experimental Method

[00155] Seventy BALB/C mice, weighing 14 ± 1 g, half male and half female, were randomly divided into 7 groups based on body weight: normal control group, model control group, Oseltamivir group, Ribavirin group, composition group, Oseltamivir + composition group, and Ribavirin + composition group, with 10 mice per group. All mice, except those in the normal control group, were lightly anesthetized with isoflurane and infected intranasally with $45 \mu\text{L}$ of 100 TCID₅₀ RSV virus solution. Treatment started on the day of infection. The gavage dose was 0.2 mL/10 g body weight per dose, once daily, for 4 consecutive days. The normal control group and model control group were treated with distilled water under the same conditions. On the 5th day, body weight was recorded for all groups, lungs were dissected and weighed, and lung tissue was collected for inflammatory factor detection. Lung index and lung index inhibition rate were calculated.

$$[00156] \text{Lung Index (\%)} = (\text{Lung Wet Weight (g)} / \text{Body Weight (g)}) \times 100$$

$$[00157] \text{Lung Index Inhibition Rate (\%)} = [(\text{Lung Weight of Model Control Group (g)} - \text{Lung Weight of Treatment Group (g)}) / (\text{Lung Weight of Model Control Group (g)} - \text{Lung Weight of Normal Control Group (g)})] \times 100$$

[00158] 4 Experimental Results

[00159] 4.1 Effects of the Composition Granules on Pulmonary Index and Pulmonary Index Inhibition Rate

[00160] The research results (Table 2) showed that after nasal infection with Respiratory Syncytial Virus (RSV) in mice, the pulmonary index in the model group was significantly elevated, showing a marked difference compared to the normal control group ($P < 0.01$). After starting treatment with the composition granules on the

day of infection for four days, the pulmonary index in the Oseltamivir phosphate group, the composition group, the Oseltamivir phosphate group + composition group, and the Ribavirin + composition group significantly decreased, with noticeable differences compared to the model control group. This indicates that the composition has an enhancing effect when combined with antiviral drugs used for upper respiratory tract infections, especially against RSV.

[00161] Table 2 Effects of the Composition Granules on Pulmonary Index in RSV-Infected Mice

Group	Dose	Animal Number (n)	Pulmonary Index (%)	Inhibition Rate (%)
Normal Control Group	-	10	0.65 ± 0.04	-
Model Control Group	-	10	0.88 ± 0.05 ##	-
Ribavirin Group	82.5 mg/kg/d	10	0.76 ± 0.03 **	0.41
Oseltamivir Phosphate Group	27.5 mg/kg/d	10	0.84 ± 0.06	0.11
Composition Group	26.4 g crude drug/kg/d	10	0.83 ± 0.05 *	0.13
Oseltamivir Phosphate + Composition Group	13.7 mg/kg/d + 13.2 g crude drug/kg/d	10	0.76 ± 0.04 **	0.45
Ribavirin + Composition Group	41.2 mg/kg/d + 13.2 g crude drug/kg/d	10	0.76 ± 0.03 **	0.43

[00162] Note: Compared with the normal control group ##P<0.01; compared with the model control group, *P<0.05.

[00163] 4.2 Effects on IL-33 Cytokine in Lung Tissue

[00164] The lung tissue was extracted from a -80°C freezer, and after treatment

with high-efficiency protein lysis buffer (containing PMSF and protease inhibitors), it was centrifuged, and the protein supernatant was collected. The protein samples were placed in an ice box and sent to Leiz Biotech Co., Ltd. for high-throughput liquid-phase protein chip detection of various cytokines in mouse lung tissue, with specific detection steps outlined in the annex.

[00165] After nasal infection with RSV, the IL-33 cytokine level in the lung tissue of the model group mice was significantly elevated, showing a marked difference compared to the normal control group ($P<0.01$). After starting treatment with the composition granules on the day of infection for four days, the IL-33 levels in the Oseltamivir phosphate group, the composition group, the Oseltamivir phosphate group + composition group, and the Ribavirin + composition group significantly decreased, with notable differences compared to the model group ($P<0.01$, $P<0.05$). See Table 3.

[00166] Table 3 Effects of the Composition Granules on Cytokine Levels in Lung Tissue of RSV-Infected Mice

Group	Dose (g crude drug/kg/d)	Animal Number (n)	Cytokine Content in Lung Tissue (pg/mL)
			IL-33
Normal Control Group	-	10	1567.11±68.24
Model Control Group	-	10	1802.2±59.65 ^{##}
Ribavirin Group	82.5 mg/kg/d	10	1495.20±351.62 [*]
Oseltamivir Phosphate Group	27.5 mg/kg/d	10	1667.23±275.1
Composition Group	26.4 g crude drug/kg/d	10	1432.25±312.4 ^{**}

Ribavirin + Composition Group	13.7 mg/kg/d +	10	1324.65±246.32**
	13.2 g crude drug/kg/d		
Oseltamivir Phosphate + Composition Group	41.2 mg/kg/d +	10	1402.26±258.64**
	13.2 g crude drug/kg/d		

[00167] Note: Compared with the normal control group ##P<0.01, #P<0.05; compared with the model group, **P<0.01.

[00168] In this study, the composition granules (26.4 g crude drug/kg/d, 1/2 dose) were administered by oral gavage to mice once per day for 3-4 consecutive days, using both Influenza Virus H1N1/FM1 strain infection models and RSV infection models, to evaluate the effectiveness of the composition granules in treating viral upper respiratory infections. The results showed that the combination of the composition with antiviral drugs reduced viral load and inflammatory cytokines in lung tissue, suggesting therapeutic effects against common specific viral infections. The use of traditional Chinese medicine in conjunction with other antiviral drugs further promotes and consolidates the antiviral effects of these medications, providing a basis for further clinical research.

[00169] Experimental Example 5: Fingerprint Chromatographic Study of the Composition of the Invention

[00170] Instruments and Reagents

[00171] Instruments: Agilent 1260 High-Performance Liquid Chromatograph (HPLC) with DAD ultraviolet detector; Agilent 1260 High-Performance Liquid Chromatograph (HPLC) with VWD ultraviolet detector; Agilent 1290 Ultra-High-Pressure Liquid Chromatograph (UHPLC) with DAD ultraviolet detector; Agilent 6538 Q-TOF-MS Mass Spectrometer with Electrospray Ionization (ESI)

source, Agilent Technologies, USA; Thermo Fisher Ultimate 3000 High-Performance Liquid Chromatograph (HPLC); Mettler Toledo XP6 Electronic Analytical Balance, Mettler-Toledo, USA; Mettler Toledo AL204 Electronic Analytical Balance, Mettler-Toledo, USA; KQ500DB Numerical Control Ultrasonic Cleaning Apparatus, Kunshan Ultrasonic Instruments Co., Ltd.; HH Digital Display Constant Temperature Water Bath, Changzhou Guoyu Instrument Manufacturing Co., Ltd.; Milli-Q Ultrapure Water System, Millipore, USA.

[00172] Reference Standards: Adenine, 99.4%, Batch No. B0002908, Beijing Manhage Biotechnology Co., Ltd.; Uridine, 99.4%, Batch No. B0008580, Beijing Manhage Biotechnology Co., Ltd.; Guanosine, 96.1%, Batch No. B0006767, Beijing Manhage Biotechnology Co., Ltd.; Inosine, 99.2%, Batch No. 140669-202007, China National Institute for the Control of Pharmaceutical and Biological Products; 5-Hydroxymethylfurfural, 95.0%, Batch No. 8610, Shanghai Shidande Standard Technology Co., Ltd.; Magnoloside A, 99.1%, Batch No. 7611, Shanghai Shidande Standard Technology Co., Ltd.; Bergaptol-O-glucopyranoside, 98%, Batch No. CFS202002, Wuhan Tianzhi Biotechnology Co., Ltd.; Nodakenin, 99.6%, Batch No. 111821-201604, China National Institute for the Control of Pharmaceutical and Biological Products; 6'-O-trans-Feruloylnodakenin, 98%, Batch No. CFS202002, Wuhan Tianzhi Biotechnology Co., Ltd.; Hydroxyphenethylanisate, 99.6%, Batch No. A05GB156933, Shanghai Yuan Ye Biotechnology Co., Ltd.

[00173] Reagents: Methanol (Merck & Co., Inc., USA, Chromatographic Grade); Acetic Acid (L07203503, Merck Millipore Technologies); other reagents are of analytical grade.

[00174] Samples: The granules prepared by the method in Preparation Example 1, with batch numbers: 200201, 200202, 200203, 200204, 200205, 200206, 200207, 200208, 200209, 200210, 200211, 200212, 200213, 200214, 200601, 200602, 200603, where the batch 200602 was used for methodological research, all provided by the Traditional Chinese Medicine R&D Department, Jiangsu Kangyuan Pharmaceutical Co., Ltd.

[00175] 1. Selection of Chromatographic Conditions

[00176] An appropriate amount of the sample was finely ground. Approximately 2g was accurately weighed and placed into a conical flask with a stopper. Then, 50 mL of water was precisely added, and the mixture was treated with ultrasound for 30 minutes. After mixing and centrifuging, the supernatant was collected as the test solution.

[00177] 1.1 Selection of Detection Wavelength

[00178] The test solution was scanned across the full wavelength range using a DAD. The results indicated that the chromatographic peaks were more abundant, the response was more uniform, and the baseline was more stable at a detection wavelength of 250 nm. Therefore, 250 nm was chosen as the characteristic detection wavelength. See Figures 4 and 5.

[00179] 1.2 Selection of Mobile Phase

[00180] Based on the water extraction process characteristics of the product, a Waters Atlantis T3 (4.6 × 250 mm, 5 μm) C18 column, which has a good separation effect on water-soluble components, was selected. The mobile phase system consisted of methanol-0.1% phosphoric acid, with a detection wavelength of 250 nm. Different

gradient mobile phase programs were tested for their separation effect. The results showed that Gradient Program IV provided better separation, appropriate retention times, and a relatively stable baseline. Therefore, Gradient Program IV was selected as the optimal mobile phase elution program. The gradient elution program is as follows. The results are shown in Figure 6.

	Time (min)	Methanol (%)	0.1% Phosphoric acid (%)
Gradient Program I	0	0	100
	5	0	100
	60	60	40
	80	100	0
Gradient Program II	0	0	100
	10	0	100
	30	15	85
	50	40	60
	80	100	0
Gradient Program III	0	0	100
	5	0	100
	25	15	85
	60	50	50
	80	100	0
Gradient Program IV	0	0	100
	5	0	100
	25	15	85
	60	55	45
	75	100	0
	80	100	0

[00181] Based on the above investigation, the chromatographic conditions are determined as follows: using octadecylsilane-bonded silica gel as the stationary phase (Waters Atlantis T3, column length 25 cm, inner diameter 4.6 mm, particle size 5 μ m); methanol as mobile phase A, and 0.1% phosphoric acid as mobile phase B, performing gradient elution as specified in the table below; flow rate is 1.0 mL/min; column temperature is 30°C; detection wavelength is 250 nm. The theoretical plate

number, based on the peak of *Apiospora radix* glycoside, should not be less than 10,000.

Time (min)	mobile phase A(%)	mobile phase B (%)
0	0	100
5	0	100
25	15	85
60	55	45
75	100	0
80	100	0

[00182] 2. Selection of Test Sample Preparation Method

[00183] To select a rational and simple method for preparing the test solution, various extraction solvents and extraction methods were investigated.

[00184] Test solution preparation: Take an appropriate amount of the sample, grind finely, take about 1 g for each of 4 portions, weigh precisely, place in a conical flask with stopper, and add 25 mL of water or 50% methanol to each portion, respectively. Ultrasonicate for 30 minutes, reflux for 30 minutes, mix well, centrifuge, and collect the supernatant, thus obtaining 4 portions of test solutions.

[00185] Results: The chromatograms obtained from the test solutions showed that, when water was used as the extraction solvent, the response of the larger polar peaks before 25 minutes was higher, and the overall chromatogram was more complex with more uniform responses. Given the characteristics of the product's water extraction process, water was preferred as the extraction solvent. The chromatograms obtained using reflux and ultrasound extraction methods showed no significant difference in peak richness or response. For convenience of operation, ultrasound extraction was preferred. Refer to Figure 7.

[00186] Based on the above investigation, the test sample preparation method is

determined as follows: take an appropriate amount of the sample, grind finely, take about 1 g, weigh precisely, place in a conical flask with stopper, add 25 mL of water, ultrasonicate (500 W, 40 kHz) for 30 minutes, mix well, centrifuge, and collect the supernatant.

[00187] 3. Durability Investigation

The effect of different wavelengths (245 nm, 250 nm, 255 nm), flow rates (0.8 mL/min, 0.9 mL/min, 1.0 mL/min, 1.1 mL/min, 1.2 mL/min), column temperatures (25°C, 28°C, 30°C, 32°C, 35°C), different batches of chromatographic columns (Column 1: Waters Atlantis T3 (4.6×250 mm, 5 μm), Serial No. 01813017014031; Column 2: Waters Atlantis T3 (4.6×250 mm, 5 μm), Serial No. 01813017014008), and instruments (Instrument 1: Agilent 1260, Instrument 2: Ultimate 3000) on the separation effect of 10 selected characteristic peaks was examined.

[00188] The results showed that, within the range of 250±5 nm wavelength, flow rates from 0.8 mL/min to 1.2 mL/min, and column temperatures from 25°C to 35°C, as well as using different batches of chromatographic columns and instruments from different brands, good separation of the selected characteristic peaks was achieved, indicating that the method has good durability. Refer to Figure 8.

[00189] 4. Method Validation

[00190] Precision Investigation: The test sample solution was prepared as described above. A 10 μL portion of the same test solution was injected six times consecutively, and the relative retention times of the 10 characteristic peaks were calculated using Nodakenin (Peak 8) as the reference peak. The results showed that the relative retention times of the 10 characteristic peaks had an RSD value of less

[illegible]

[00194] Table 5: Calculation Results of Reproducibility Investigation of Characteristic Chromatogram

Peak NO.	Relative Retention Time (min)						RSD (%)
	1	2	3	4	5	6	
Peak 1	0.103	0.103	0.103	0.103	0.103	0.103	0.33
Peak 2	0.252	0.251	0.251	0.251	0.250	0.251	0.15
Peak 3	0.338	0.337	0.337	0.337	0.336	0.337	0.14
Peak 4	0.355	0.355	0.355	0.355	0.354	0.355	0.11
Peak 5	0.397	0.397	0.397	0.397	0.396	0.397	0.08
Peak 6	0.840	0.840	0.840	0.840	0.840	0.840	0.01
Peak 7	0.922	0.922	0.922	0.922	0.922	0.922	0.01
Peak 8							
(S)	1.000	1.000	1.000	1.000	1.000	1.000	0.00
Peak 9	1.188	1.188	1.188	1.188	1.188	1.188	0.01
Peak 10	1.285	1.285	1.285	1.285	1.285	1.285	0.01

[00195] Table 6: Calculation Results of Stability Investigation of Characteristic Chromatogram

Peak NO.	Relative Retention Time (min)									RSD (%)
	0h 36h	3h	6h	9h	12h	18h	24h	30h		
Peak 1	0.104	0.104	0.104	0.103	0.103	0.103	0.103	0.103	0.103	0.40
Peak 2	0.251	0.251	0.252	0.251	0.250	0.251	0.251	0.251	0.251	0.16
Peak 3	0.337	0.338	0.338	0.337	0.336	0.337	0.338	0.337	0.337	0.16
Peak 4	0.355	0.355	0.356	0.355	0.354	0.355	0.355	0.354	0.355	0.13
Peak 5	0.397	0.397	0.398	0.397	0.396	0.397	0.397	0.397	0.397	0.09
Peak 6	0.840	0.840	0.840	0.840	0.840	0.840	0.840	0.840	0.840	0.01
Peak 7	0.922	0.922	0.922	0.922	0.922	0.922	0.922	0.922	0.922	0.01
Peak 8										
(S)	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	0.00
Peak 9	1.188	1.188	1.188	1.188	1.188	1.188	1.188	1.188	1.188	0.01
Peak 10	1.285	1.285	1.285	1.285	1.285	1.285	1.285	1.285	1.285	0.02

[00196] 5. Multi-Batch Determination and Characteristic Chromatogram Generation

[00197] The determination of 14 batches of clinical practice samples, 3 batches of

pilot-scale samples, and 3 batches of process validation samples was conducted according to the above methods. Ten peaks were selected as characteristic peaks, and a reference fingerprint chromatogram was generated based on 20 batches of formulations. The peak corresponding to the reference peak of Nodakenin was designated as Peak S. The relative retention times of each characteristic peak were calculated, and each peak should be within $\pm 10\%$ of the specified value. The specified values are as follows: 0.11 (Peak 1), 0.27 (Peak 2), 0.36 (Peak 3), 0.38 (Peak 4), 0.41 (Peak 5), 0.84 (Peak 6), 0.92 (Peak 7), 1.00 (Peak 8), 1.19 (Peak 9), and 1.29 (Peak 10). The multi-batch results are shown in Figure 12, and the reference characteristic chromatogram is shown in Figure 13.

[00198] Table 7: Relative Retention Time Results for 20 Batches of Formulations

Batch NO.	Peak 1	Peak 2	Peak 3	Peak 4	Peak 5	Peak 6	Peak 7	Peak 8	Peak 9	Peak 10
200201	0.114	0.270	0.356	0.372	0.411	0.841	0.923	1.000	1.187	1.285
200202	0.114	0.270	0.356	0.372	0.411	0.841	0.923	1.000	1.187	1.285
200203	0.113	0.270	0.356	0.372	0.411	0.841	0.923	1.000	1.187	1.285
200204	0.113	0.270	0.356	0.372	0.411	0.841	0.923	1.000	1.187	1.285
200205	0.113	0.270	0.355	0.371	0.410	0.841	0.923	1.000	1.187	1.285
200206	0.113	0.270	0.355	0.371	0.410	0.841	0.923	1.000	1.187	1.285
200207	0.113	0.269	0.355	0.371	0.410	0.841	0.923	1.000	1.187	1.285
200208	0.113	0.270	0.355	0.371	0.410	0.841	0.923	1.000	1.187	1.285
200209	0.113	0.270	0.355	0.371	0.410	0.841	0.923	1.000	1.187	1.285
200210	0.113	0.270	0.355	0.371	0.410	0.841	0.923	1.000	1.187	1.285
200211	0.113	0.269	0.355	0.371	0.410	0.841	0.923	1.000	1.187	1.285
200212	0.113	0.270	0.355	0.372	0.410	0.841	0.923	1.000	1.187	1.285
200213	0.113	0.270	0.355	0.371	0.410	0.841	0.923	1.000	1.187	1.285
200214	0.113	0.270	0.355	0.371	0.410	0.841	0.923	1.000	1.187	1.284

200601	0.113	0.269	0.354	0.371	0.410	0.841	0.923	1.000	1.187	1.285
200602	0.113	0.270	0.355	0.371	0.410	0.841	0.923	1.000	1.187	1.285
200603	0.113	0.270	0.355	0.371	0.410	0.841	0.923	1.000	1.187	1.285
210401	0.117	0.268	0.352	0.369	0.409	0.84	0.922	1.000	1.194	1.300
210402	0.117	0.268	0.352	0.369	0.409	0.84	0.922	1.000	1.194	1.300
210403	0.117	0.269	0.352	0.37	0.409	0.84	0.922	1.000	1.194	1.300

[00199] 6. Characteristic Chromatogram Quality Standards

[00200] Chromatographic Conditions and System Suitability Test: The stationary phase was octadecylsilane-bonded silica gel (Waters Atlantis T3, column length 25 cm, inner diameter 4.6 mm, particle size 5 μ m); the mobile phase A was methanol, and mobile phase B was 0.1% phosphoric acid. Gradient elution was carried out according to the specified conditions in the table below; the flow rate was 1.0 mL/min; the column temperature was 30° C; and the detection wavelength was 250 nm. The theoretical plate count should be no less than 10,000, based on the Nodakenin peak.

Time (min)	mobile phase A(%)	mobile phase B (%)
0	0	100
5	0	100
25	15	85
60	55	45
75	100	0
80	100	0

[00201] Preparation of Reference Solution: An appropriate amount of Nodakenin reference substance was precisely weighed, and 50% methanol was added to prepare a solution containing 0.15 mg of the reference substance per 1 mL.

[00202] Preparation of Test Solution: An appropriate amount of the sample was

finely powdered. Approximately 1 g of the sample was precisely weighed and placed into a conical flask with a stopper. 25 mL of water was added precisely, and the mixture was sonicated (power 500W, frequency 40kHz) for 30 minutes. The mixture was shaken well, centrifuged, and the supernatant was collected.

[00203] Determination Method: Precise aliquots of 10 μ L of both the reference solution and the test solution were injected into the liquid chromatograph for analysis, and the chromatograms were recorded.

[00204] The characteristic chromatogram of the test solution should display 10 characteristic peaks, with the peak corresponding to the reference substance peak designated as Peak S. The relative retention times of each characteristic peak should be within $\pm 10\%$ of the specified values. The specified relative retention times are as follows: 0.11 (Peak 1), 0.27 (Peak 2), 0.36 (Peak 3), 0.38 (Peak 4), 0.41 (Peak 5), 0.84 (Peak 6), 0.92 (Peak 7), 1.00 (Peak 8 [S]), 1.19 (Peak 9), and 1.29 (Peak 10). The reference characteristic chromatogram is shown in Figure 14.

[00205] The above is only the preferred embodiment of the present invention. It should be pointed out that those skilled in the art, without departing from the principles of the present invention, may make various improvements and modifications, which should also fall within the scope of protection of the present invention.

What is claimed is:

1. A Traditional Chinese Medicine extract, wherein, by weight ratio, the extract is made from the following ingredients: *Magnoliae Officinalis* Cortex 1-100 parts, *Arecae Semen* 1-100 parts, *Amomum tsaoko* Crevost & Lem. 1-100 parts, *Ephedrae Herba* 1-100 parts, *Armeniacae Semen Amarum* 1-100 parts, *Notopterygii Rhizoma et Radix* 1-100 parts, *Zingiberis Rhizoma* 1-100 parts, *Pogostemonis Herba* 1-100 parts, *Eupatorium fortunei* Turcz. 1-100 parts, *Atractylodis Rhizoma* 1-100 parts, *Poria cocos* 1-100 parts, *Atractylodis Macrocephalae Rhizoma* 1-100 parts, *Gypsum Fibrosum* 1-100 parts, *Crataegi Fructus* 1-100 parts, *Massa Medicata Fermentata* 1-100 parts, *Hordei Fructus Germinatus* 1-100 parts, *Pheretima* 1-100 parts, *Vincetoxicum pycnostelma* Kitag. 1-100 parts, *Dryopteridis Crassirhizomatis Rhizoma* 1-100 parts, and *Lepidium apetalum* seeds 1-100 parts; wherein, the extract has an ephedrine content of 0.5-1.5 mg/g and a solid content transfer rate of 18-25%.
2. The Traditional Chinese Medicine extract according to claim 1, wherein the extract is made from the following ingredients: *Magnoliae Officinalis* Cortex 1-80 parts, *Arecae Semen* 1-80 parts, *Amomum tsaoko* Crevost & Lem. 1-80 parts, *Ephedrae Herba* 1-60 parts, *Armeniacae Semen Amarum* 1-60 parts, *Notopterygii Rhizoma et Radix* 1-80 parts, *Zingiberis Rhizoma* 1-60 parts, *Pogostemonis Herba* 1-80 parts, *Eupatorium fortunei* Turcz. 1-60 parts, *Atractylodis Rhizoma* 1-80 parts, *Poria cocos* 1-160 parts, *Atractylodis Macrocephalae Rhizoma* 1-120 parts, *Gypsum Fibrosum* 1-80 parts, *Crataegi Fructus* 1-50 parts, *Massa Medicata Fermentata* 1-80 parts, *Hordei Fructus Germinatus* 1-60 parts, *Pheretima* 1-80 parts, *Vincetoxicum pycnostelma* Kitag. 1-80 parts, *Dryopteridis Crassirhizomatis Rhizoma* 1-60 parts, and *Lepidium apetalum* seeds 1-80 parts, wherein, the

extract has a content of Nodakenin ranging from 2-8 mg/g.

3. The Traditional Chinese Medicine extract according to claim 1 or 2, wherein the extract is made from the following ingredients: *Magnoliae Officinalis* Cortex 30-50 parts, *Arecae Semen* 20-30 parts, *Amomum tsaoko* Crevost & Lem. 30-50 parts, *Ephedrae Herba* 20-30 parts, *Armeniacae Semen Amarum* 20-30 parts, *Notopterygii Rhizoma et Radix* 30-50 parts, *Zingiberis Rhizoma* 30-50 parts, *Pogostemonis Herba* 30-50 parts, *Eupatorium fortunei* Turcz. 20-30 parts, *Atractylodis Rhizoma* 30-50 parts, *Poria cocos* 120-150 parts, *Atractylodis Macrocephalae Rhizoma* 80-100 parts, *Gypsum Fibrosum* 30-50 parts, *Crataegi Fructus* 20-30 parts, *Massa Medicata Fermentata* 30-50 parts, *Hordei Fructus Germinatus* 20-30 parts, *Pheretima* 30-50 parts, *Vincetoxicum pycnostelma* Kitag. 30-50 parts, *Dryopteridis Crassirhizomatis Rhizoma* 20-30 parts, and *Lepidium apetalum* seeds 30-50 parts.

4. The Traditional Chinese Medicine extract according to claim 3, wherein the extract is made from the following ingredients: *Magnoliae Officinalis* Cortex 50 parts, *Arecae Semen* 30 parts, *Amomum tsaoko* Crevost & Lem. 30 parts, *Ephedrae Herba* 20 parts, *Armeniacae Semen Amarum* 30 parts, *Notopterygii Rhizoma et Radix* 50 parts, *Zingiberis Rhizoma* 50 parts, *Pogostemonis Herba* 50 parts, *Eupatorium fortunei* Turcz. 30 parts, *Atractylodis Rhizoma* 50 parts, *Poria cocos* 150 parts, *Atractylodis Macrocephalae Rhizoma* 100 parts, *Gypsum Fibrosum* 50 parts, *Crataegi Fructus* 30 parts, *Massa Medicata Fermentata* 30 parts, *Hordei Fructus Germinatus* 30 parts, *Pheretima* 50 parts, *Vincetoxicum pycnostelma* Kitag. 50 parts, *Dryopteridis Crassirhizomatis Rhizoma* 30 parts, and *Lepidium apetalum* seeds 50 parts.

5. The Traditional Chinese Medicine extract according to any of claims 1-4, wherein the

preparation of the extract includes the following steps: Weigh *Magnoliae Officinalis* Cortex, *Arecae Semen*, *Amomum tsaoko* Crevost & Lem., *Ephedrae Herba*, *Armeniacae Semen Amarum*, *Notopterygii Rhizoma et Radix*, *Zingiberis Rhizoma*, *Pogostemonis Herba*, *Eupatorium fortunei* Turcz., *Atractylodis Rhizoma*, *Poria cocos*, *Atractylodis Macrocephalae Rhizoma*, *Gypsum Fibrosum*, *Crataegi Fructus*, *Massa Medicata Fermentata*, *Hordei Fructus Germinatus*, *Pheretima*, *Vincetoxicum pycnostelma* Kitag., *Dryopteridis Crassirhizomatis Rhizoma*, and *Lepidium apetalum* seeds. Extract them twice with water, adding six times the amount of water for the first extraction and extracting for 1.5 hours, then adding four times the amount of water for the second extraction and extracting for 1.0 hour. Combine the extracts, filter, and concentrate the filtrate to a relative density of 1.10-1.15. Centrifuge and filter the solution, then dry the filtrate. The extract contains 1.20-1.50 mg/g of ephedrine, a solid content transfer rate of 19-22%, and 6-8 mg/g of Nodakenin.

6. The Traditional Chinese Medicine extract according to claim 5, wherein the preparation of the traditional Chinese medicine extract includes: weighing 15g of *Magnoliae Officinalis* Cortex, 9g of *Arecae Semen*, 9g of *Amomum tsaoko* Crevost & Lem., 6g of *Ephedrae Herba*, 9g of *Armeniacae Semen Amarum*, 15g of *Notopterygii Rhizoma et Radix*, 15g of *Zingiberis Rhizoma*, 15g of *Pogostemonis Herba*, 9g of *Eupatorium fortunei* Turcz., 15g of *Atractylodis Rhizoma*, 45g of *Poria cocos*, 30g of *Atractylodis Macrocephalae Rhizoma*, 15g of *Gypsum Fibrosum*, 9g of *Crataegi Fructus*, 9g of *Massa Medicata Fermentata*, 9g of *Hordei Fructus Germinatus*, 15g of *Pheretima*, 15g of *Vincetoxicum pycnostelma* Kitag., 9g of *Dryopteridis Crassirhizomatis Rhizoma*, and 15g of *Lepidium apetalum* seeds; Extract them twice with water, adding six times the amount of water for the first extraction and extracting for 1.5 hours, then adding four times the amount of water for the second extraction and extracting

for 1.0 hour. Combine the extracts, filter, and concentrate the filtrate to a relative density of 1.10-1.15. Centrifuge and filter the solution, then dry the filtrate.

7. The use of the extract according to any one of claims 1-6 in the preparation of a drug for treating H1N1 influenza virus or FM1, or respiratory syncytial virus.

8. A drug made by combining the traditional Chinese medicine extract according to any of claims 1-6 with pharmaceutically acceptable excipients or additives.

9. The drug according to claim 6, wherein the drug is in the form of granules, and the excipients or additives are preferably dextrin and sucralose.

10. A method for detecting the fingerprint chromatogram of the extract according to any of claims 1-6 or drug according to claim 6, wherein, a sample solution is subjected to HPLC analysis, where the chromatographic conditions for HPLC include: the use of a C18 chromatographic column, methanol as mobile phase A, and a 0.1% aqueous phosphoric acid solution as mobile phase B. The elution in the HPLC detection follows a gradient elution program as follows: 0~5 min, 0% A; 5~25 min, 0%~15% A; 25~60 min, 15%~55% A; 60~75 min, 55%~100% A; 75~80 min, 100% A.

11. The method according to claim 10, wherein, the chromatographic conditions include: a flow rate of 1.0 mL/min, a column temperature of 30° C, and a detection wavelength of 250 nm.

12. The method according to claim 10 or 11, wherein, the characteristic chromatogram of the sample should show 10 characteristic peaks, with the corresponding peak for the reference peak being peak S. The relative retention time of each characteristic peak to peak S should be within $\pm 10\%$ of the specified value, preferably within 5%. The specified relative retention times are as follows: 0.11 (Peak 1), 0.27 (Peak 2), 0.36 (Peak 3), 0.38

(Peak 4), 0.41 (Peak 5), 0.84 (Peak 6), 0.92 (Peak 7), 1.00 [Peak 8 (S)], 1.19 (Peak 9), 1.29 (Peak 10).