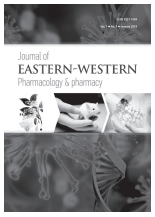

Original Article

https://doi.org/10.64269/jewpp.v6i1.4215

Journal of
EASTERN-WESTERN
Pharmacology & pharmacy

The formulation and evaluation of antiviral herbal tablet Chun-7

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KEYWORDS

Herbal tablets; Tablet formulation; Granule properties, Qualification, Quantification

Received: 2024/11/19 Accepted: 2024/12/17
Revised: 2024/11/30 Published: 2024/01/30

ABSTRACT

This study explores the formulation and evaluation of Chun-7 antiviral herbal tablets derived from a traditional Mongolian medicinal blend. The objective was to develop a tablet form to enhance the convenience and efficacy of Chun-7, traditionally used for respiratory tract viral infections. The Chun-7 formulation includes seven medicinal plants known for their pharmacological properties. Tablets were prepared using the wet granulation method, with granules adjusted to different moisture levels (2%, 4%, 6%, and 8%) to evaluate their impact on tablet characteristics. The tablets were assessed for weight variation, hardness, friability, and disintegration time. Results indicated that the maximum weight variation was 3.62%, within acceptable limits. Tablets with 5% and 6% granule moisture content exhibited optimal hardness (1.11 and 1.08 MPa, respectively) and acceptable friability. The qualitative and quantitative analysis methods were modified, and requirements were evaluated according to Mongolian National Pharmacopoeia. Total alkaloids and phenolic content were 1.2 mg and 8 mg, respectively. The study underscores the importance of moisture content in granule preparation, influencing the tablets' physical, chemical, and mechanical properties. This research provides a viable alternative to traditional herbal powder formulations, enhancing dosage accuracy and patient compliance. Further studies are recommended to evaluate the clinical efficacy and long-term stability of Chun-7 tablets under varied storage conditions.

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INTRODUCTION

In light of the persistent challenge posed by respiratory tract viral infections and the emerging need for alternative therapeutic approaches, there is a growing importance to explore the potential of traditional herbal drugs as a viable treatment method for the most frequently occurring infectious viral illnesses in all age groups globally.[1] In Mongolian traditional medical scripture, the "Chun-7" herbal drug is indicated for its antiviral effects in treating pneumonia, respiratory tract inflammations, lung heat, cough, and symptoms of viral infections. The application of Chun-7 herbal drug in treating acute respiratory tract infections caused by the influenza A virus and SARS-CoV-2 (COVID-19) has been validated through preclinical studies. This herbal drug exhibits significant potential in enhancing the immune response, reducing pulmonary fibrosis, and inhibiting the proliferation of lung MRC-5 fibroblast cells, thereby preventing the formation of fibrotic tissue. Notably, these effects are attributed to the suppression of inflammatory cytokines, including IL-13, IL-1, and particularly IL-6, resulting in a substantial reduction of 2.8 pg/mL and a remarkable 44.3% decrease in inflammation.

The Chun-7 traditional powder medicine combines seven medicinal plants: *Sophorae flavescens* Ait., *Rheum undulatum* L., *Glehnia littoralis* F.Schmidt ex Miq., *Saposhnikovia divaricata* (Turcz.) Schischk., *Astragalus mongolicus* Bunge., *Zingiber officinale* Rosc., and *Aconiti Kusnezoffii* radix cocta. Each plant in this formulation offers distinct pharmacological properties. *Sophorae flavescens* Ait. exhibits anti-inflammatory and antimicrobial effects.[2,3] *Rheum undulatum* L. is recognized for its laxative properties and potential benefits for the digestive system, pulmonary system dysfunctions, and disorders related to the reproductive system.[4] *Glehnia littoralis* F.Schmidt ex Miq. is utilized in traditional Chinese medicine to support respiratory health.[5] *Saposhnikovia divaricata* (Turcz.) Schischk. is valued for its anti-inflammatory, antioxidant, immunoregulatory, and analgesic activities.[6] *Astragalus mongolicus* Bunge. enhances immune function and has anti-fibrosis properties.[7,8] *Zingiber officinale* Rosc offers anti-inflammatory, anticoagulant, antioxidant, antimicrobial, and digestive benefits.[9,10] *Aconiti Kusnezoffii* radix cocta prepared aconite root is cautiously employed for pain relief and inflammatory conditions after processing to remove its toxic properties.[11] The combination of these plants likely produces a synergistic therapeutic effect.

The primary focus of this study is the formulation and evaluation of Chun-7 tablets derived from the radix and rhizoma parts of medicinal plants. The original Chun-7 powder drug presents challenges in dispensing and consumption, leading to an exploration of tablet formulation as a viable alternative. The oral route of tablet drug administration is considered the predominant and efficacious method for conventional drug delivery, offering notable advantages such as convenience, ease of administration, flexibility in dosage form design, simplified production, and cost-effectiveness. This research aims to contribute to the advancement of pharmaceutical science by addressing practical concerns associated with herbal medicine administration while leveraging the benefits offered by tablet formulations.

MATERIALS AND METHODS

Plant materials

Five of the seven medicinal plants (*Sophorae flavescens* Ait., *Rheum undulatum* L., *Glehnia littoralis* F.Schmidt ex Miq., *Zingiber officinale* Rosc., and *Aconiti Kusnezoffii* radix cocta) used in the study were purchased from the Hebei Anjia Pharmaceutical Co., Ltd, Inner Anguo Bangbiao Traditional Chinese Medicine Pieces Co., Ltd,. *Astragalus mongolicus* Bunge. and *Saposhnikovia divaricata* (Turcz.) Schichk. were collected from Tuv province, Mongolia. The dried roots of all selected plants were authenticated and analyzed using the standards outlined in the Chinese Pharmacopoeia, Japanese Pharmacopoeia, and Mongolian National Pharmacopoeia.

Preparation of the plant materials

The seven plant materials were processed by crushing and grinding, followed by sieving through two different mesh sizes (40 mesh and 80 mesh) to evaluate the impact of particle size on the characteristics of the tablets. The herbal powders obtained from both sieving processes were thoroughly mixed to ensure uniformity.

Preparation and evaluation of pre-compressional Chun-7 herbal granule

The Chun-7 herbal tablets were prepared using a systematic approach involving the wet granulation method, which is known to improve powders' compaction and flow properties.[12] The process began with the thorough mixing of the powdered plant materials to ensure a uniform distribution of active ingredients. Subsequently, the herbal blend underwent wet granulation with 30% ethanol as the binding agent. Ethanol was selected due to its ability to act as a solvent for many herbal constituents, enhancing the cohesion among the powder particles.[13] The granulation process involved adding ethanol to the herbal powder blend while continuously mixing to achieve a homogeneous wet mass. The wet granules were then dried to four different moisture levels: 2%, 4%, 6%, and 8%. This step evaluated the impact of granule moisture content on the final tablet characteristics, such as hardness, disintegration time, and friability. Moisture content in granules can significantly influence the tablet's mechanical strength and stability.[14] After drying, the granules were sized through a sieve to ensure uniform particle size distribution, which is crucial for consistent tablet quality. The dried granule's pre-compressional parameters of the herbal blend were evaluated to ensure the blend exhibited suitable flow properties and compressibility, which are critical for the tablet formulation process. Then, the granules were compressed into tablets using a tablet press. The compression parameters, such as pressure and dwell time, were optimized to produce tablets with desired properties, including uniform weight, adequate hardness, and minimal friability.

Bulk density

This parameter was determined by measuring the mass of the powder and dividing it by its volume without any tapping or external compaction. Bulk density indicates the powder's packing efficiency and potential storage requirements. It was measured by filling a graduated cylinder with the herbal powder without tapping and recording the volume and weight.

Tapped density

Tapped density was measured to assess how much the powder could be compacted under standardized tapping conditions. This process involved filling a graduated cylinder with the herbal powder and subjecting it to a series of taps using a tapped density tester until no further volume reduction was observed. The mass of the powder was then divided by the final tapped volume. This parameter helps understand the degree of consolidation and compaction of the powder.

Carr's index (compressibility)

Carr's Index was calculated to quantify the powder's flowability and compressibility. It is determined using the equation 1.

$$Carr's\ index = \left(\frac{Tapped\ density - Bulk\ density}{Tapped\ density}\right) \times 100 \quad (1)$$

A lower Carr's Index indicates better flowability, whereas a higher value suggests poor flow properties and potential difficulties in tablet formulation. This index provides insight into the potential challenges during the tablet manufacturing process, such as powder flow through the hopper or die filling.[15]

Hausner's ratio

Hausner's Ratio was calculated as the ratio of tapped density to bulk density by equation 2.

$$Hausner's\ ratio = \frac{Tapped\ density}{Bulk\ density} \quad (2)$$

This ratio is another indicator of flow properties, with values close to 1 indicating excellent flow and higher values indicating poor flowability. A Hausner's Ratio greater than 1.25 typically suggests poor flow characteristics, which may require the addition of flow aids or modifications to the formulation process.[15]

Physicochemical evaluation

Physicochemical evaluation of Chun-7 tablet was performed according to the general requirements for tablet of Mongolian national pharmacopoeia. As for the physical parameters including weight variation, hardness, friability and disintegration. Identification of active pharmaceutical ingredients of each raw material, content of total alkaloids, phenolic compounds were tested for chemical evaluation. Microbial contamination of Chun-7 tablet were tested as non-sterile pharmaceutical finished products.

Tablet hardness

Tablet breaking force was determined individually with a Biobase THT-3 tablet hardness tester; the following ten tablets were used, and the mean crushing strength was calculated in MPa. Tablet breaking force's criteria between 0.45 – 1.2 MPa is the standard for tablets, according to Mongolian National Pharmacopeia.[16]

Friability test

The friability test is carried out using the Friability apparatus. The weighted tablets are placed in the apparatus and rotated at 25 rpm for 4 minutes. After an interval, tablets are taken out from the apparatus, and once again, they are weighed. Friability is calculated using the equation 3, and the result should be higher than 97% to ensure that the tablets are susceptible to capping, abrasion, or breakage during storage, transportation, packaging, and handling prior to usage.

$$Friability = \frac{Initial\ weight - Final\ weight}{Initial\ weight} \times 100 \quad (3)$$

Disintegration time

Six Chun-7 herbal tablets were randomly selected to determine the disintegration time. The acidic buffer (pH 1.2) was used as a disintegration medium, and the temperature was maintained at 37±0.5 °C. The average disintegration time of six tablets was noted down for calculation.[17]

Average weight and uniformity of weight

Twenty tablets were weighed individually using an analytical balance, and the average weight was calculated. Each tablet's weight was compared and calculated using the equation 4. According to MNP, uniformity of weight should not exceed ±5%.[16]

$$Uniformity\ of\ weight, \% = \left(\frac{Average\ weight - Individual\ weight}{Average\ wegith}\right) \times 100 \quad (4)$$

Identification

Each active compound of raw materials was detected in the Chun-7 tablet using the TLC method. Uniform powder of ground 30 tablets was used for sample preparations as prescribed in according to Chinese and Japanese pharmacopoeias.[17,18] The TLC study was conducted on precoated aluminum-backed silica gel 60 F_{254} plates. Suitable mobile phases and detection were selected according to the monographs of each raw material, shown in Table 1. Active compounds from *Sophorae flavecens, Rheum undulatum, Saposhnikovia divaricata, Zingiberis officinale* were detected as prescribed by the individual monographs of Chinese pharmacopoeia. Additionally, active compounds from *Aconitum kusnezoffi* and *Astragalus mongolicus* were identified in accordance with the monographs of the Japanese pharmacopoeia. In 2013, Xing Su et al., isolated β-sitosterol from *Glehnia littoralis*. Thus, the TLC method for specified in the *Typhonii* rhizome of Chinese pharmacopoeia was used to detect β-sitosterol.

Table 1. TLC system for each herbal material consisting Chun-7 tablet.

Marker compound	Mobile phase	Detection	Reference
Matrine	Toluene, acetone, methanol 8:3:0.5 Toluene, ethylacetate, methanol, water 2:4:2:1 (<10°C)	In visible light (with spray of Dragendorf's reagent and sodium nitrite solution)	Sophorae flavencens, Chinese pharmacopoeia 2020
Aconitine, benzoylaconitine, benzoylmesaconitine, benzoylhypaconitine	Ethylacetate, ethanol, ammonia (28%) 40:3:2	In visible light (with spray of Dragendorf's reagent and sodium nitrite solution)	Processed Aconite root, Japanese pharmacopoeia, 18
Rhein	Petroleum ether, ethylacetate, formic acid 15:5:1	In 365 nm of UV light	Rhei radix, Chinese pharmacopoeia, 2020
Prim-o-glycosylcimifugin	Chloroform, methanol 4:1	In 254 nm of UV light	Saposhnikoviae radix, Chinese pharmacopoeia, 2020
β-sitosterol	Chloroform, acetone 25:1	In 365 nm of UV light (with spray of sulfuric acid solution and heat at 105°C)	Typhonii rhizome, Chinese pharmacopoeia, 2020
Astragaloside IV	Ethylacetate, methanol, water 20:5:4	In 365 nm of UV light (with spray of sulfuric acid solution and heat at 105°C)	Astragalus root, Japanese pharmacopoeia, 18
6-gingerol	Petroleum ether, chloroform, ethylacetate 2:1:1	In visible light (with spray of vanillin sulfuric acid solution and heat at 105°C)	Zingiberis rhizome recens, Chinese pharmacopoeia, 2020

Quantification of the total alkaloid content

According to Mongolian traditional medicine pharmacopeia, the UV-Vis spectrophotometric method of Norov-7 traditional medicine was used to determine the total content of alkaloids.

Reference solution: Dissolved a quantity of matrine chemical reference standard, accurately weighed, in distilled water to produce a 100 micrograms per ml solution.

Reagent preparation: Bromocresol green (BCG) solution was prepared by dissolving 69.8 mg of bromocresol green in 1000 mL of distilled water by adding 3 mL of 2M NaOH for better solubility. The phosphate buffer (pH 4.7) was prepared by dissolving 71.6 gm of disodium hydrogen phosphate in 1 L distilled water (adjusted pH 4.7 with 20% phosphoric acid). Sample solution: 30 tablets of Chun-7 were ground to a uniform powder. To 1 gram of powder, 50 ml of methanol was added, heated under reflux for 1 hour, cooled, and filtered. The filtrate was transferred to a round-bottomed flask and evaporated using a rotary evaporator under vacuum at a temperature of 45 °C to dryness. The residue was then dissolved in 2M HCl and filtered into the 50 mL volumetric flask.

Procedure: Measure 1 ml of the sample solution in a separatory funnel, add 5 ml each of BCG solution and phosphate buffer, and mix thoroughly. The color of the mixed solution should be cyan blue (add 2M NaOH till cyan blue). The mixture was extracted 4 times using 4 mL of chloroform and vigorously shaken for 30 seconds.

The organic phase was separated and dehydrated by passing over anhydrous sodium sulfate, then transferred to a 25 mL volumetric flask and filled with chloroform up to the mark.

Then, proceed in the same manner with 1 mL of standard solution. The test solutions were analyzed

using a UV-Vis spectrophotometer at a wavelength of 415 nm with chloroform as a blank and the quantity of total alkaloid calculated as a matrine equivalent.[19]

Quantification of the total phenolic compound content

The Folin-Ciocalteu colorimetric method based on an oxidation-reduction reaction was used to determine the total content of the phenolic compound present in the Chun-7 tablet.

Reference solution: Dissolved a quantity of gallic acid chemical reference standard, accurately weighed, in 70% ethanol to produce a 100 micrograms per ml solution.

Sample solution: To 0.3 grams of powder mentioned in the quantification of total alkaloids, 40 ml 70% ethanol was added, ultrasonicated for 15 minutes, cooled, filtered into 50 ml volumetric flask, and filled with the same diluent up to the mark.

Procedure: Measured 0.5 ml of sample solution transferred to 25 ml volumetric flask, added 9 ml of distilled water and 1 ml of Folin-Ciocalteu reagent vigorously shaken and still for 15 minutes. Then, 10 ml of 7% sodium carbonate solution was added, vigorously shaken, and filled with distilled water up to the mark. After 90 minutes, test solutions were analyzed using a UV-Vis spectrophotometer at a wavelength of 750 nm, and the quantity of total phenolics was calculated as a gallic acid equivalent. As a blank determination, 0.5 ml of distilled water and 0.5 ml of standard solution were performed in the same manner, separately.[16]

Validation of analytical method

Analytical methods were validated using the guidelines of the International Conference on Harmonization (Q2)R1. The validation parameters investigated were the linearity, selectivity, accuracy, precision, detection, and quantification limits.

The linear relationship was evaluated for the six concentrations of standard solution. The calibration curve with concentration versus absorbance was plotted, and the obtained data were subjected to regression.

The accuracy of analytical procedures was assessed using nine determinations over three concentration levels (50%, 100%, 150%) of sample solution. Accuracy was reported as the percent recovery by the difference between the mean, accepted true value, and confidence intervals.

Repeatability and intermediate precision were investigations of precision. Repeatability was assessed using ten determinations at 100% of the test concentration, and intermediate precision was assessed using ten determinations on different days.

The limit of detection (LOD), and limit of quantification (LOQ) were determined separately based on the standard deviation of the y-intercept and slope of the calibration curve by using the equation 5 and 6, respectively.[20]

$$LOD = \frac{3.3\delta}{S} \quad (5) \qquad LOQ = \frac{10\delta}{S} \quad (6)$$

Where, δ - standard deviation of y-intercept; S - slope of calibration curve;

Microbial test

Total aerobic microbial, total yeast, mold, and Bile-tolerant gram-negative bacteria counts, *Escherichia coli, and Salmonella* were tested according to MNP as Botanicals not to be prepared at high temperatures. Ground 30 units of Chun-7 tablet into uniform powder. Dissolved 10 g of the powder in pH 6.8-7.0 Phosphate Buffer to made 100 mL, as initial 1:10 dilution. Diluted the initial dilution until suspension had obtained (1:100, 1:1000, 1:10000 and 1:100000), performed the test for absence of inhibitory as described in Table 2.[21]

Table 2. Conditions of tests for microbial contamination of Chun-7 tablet.

Microbial test	Tested dilution	Medium	Incubation temperature	Incubation time
Total aerobic microbial	1:10, 1:100, 1:1000, 1:10000, 1:100000	Soybean-Casein Digest Agar	30-35°C	3-5 days
Total yeast and mold	1:10, 1:100, 1:1000, 1:10000	Sabouraud Dextrose Agar	20-25°C	5-7 days
Bile-tolerant gram-negative bacteria	1:10, 1:100, 1:1000, 1:10000	Soybean-Casein Digest Agar	30-35°C	24-48 hours
Escherichia coli	1:10	Soybean-Casein Digest Agar	30-35°C	18-24 hours
Salmonella	1:10	Soybean-Casein Digest Agar	30-35°C	18-24 hours

RESULTS

Formulation and characterization of Chun-7 tablet

The primary characterization and properties of granules containing Chun-7 herbal powder used for preparing tablets are mentioned in Table 3.

Granules with 5% moisture content showed excellent flow properties (Hausner's ratio 1.00, Carr's index 0%), while those with 6% moisture demonstrated good flow properties (Hausner's ratio 1.18, Carr's index 15%). Both are suitable for tablet compression, with the 5–6% moisture range being optimal.

Table 3. Properties of pre-compressional Chun-7 herbal granule

Granule moisture %	Bulk density (gm/ml)	Tapped density (gm/ml)	Carr's index %	Hausner ratio
4 %	0.5	0.67	27	1.35
5 %	0.55	0.55	0	1.00
6 %	0.48	0.56	15	1.18
9 %	0.5	0.78	34	1.56

The physical properties of the compressed Chun-7 herbal tablets were evaluated in **Table 4.**

Table 4. Physical properties of Chun-7 herbal tablets compressed with different granule moistures

Tablet granule moisture %	Average weight (g, ±%)	Hardness (MPa)	Friability (%)	Disintegration time (min)
4 %	0.5 (+3.62; -2.64)	0.55	98.9	12
5 %	0.5 (+2.26; -3.45)	1.11	100	8
6 %	0.5 (+2.26; -3.45)	1.08	99.7	8
9 %	0.5 (+2.26; -3.45)	0.3	99.1	8

The maximum weight variation observed was 3.62%, which is acceptable. The hardness of the tablets compressed with 5% and 6% granule moisture were 1.11 and 1.08 MPa, respectively, deemed most acceptable. The friability of the tablets compressed with 5% and 6% granule moisture was 100% and 99.7%, respectively, demonstrating acceptable resistance to mechanical stress during handling. Tablets with 5% and 6% granule moisture also exhibited the shortest disintegration time of 8 minutes, highlighting their suitability for immediate-release formulations.

This ties into the optimal properties of granules with 5–6% moisture content and reinforces their practical application in tablet formulation.

Qualitative analysis of Chun-7 tablet

Based on the results of pre-compressional and physical properties, tablet with 6% moisture were contemplated most prominent. Hence, chemical and microbial assessments were further investigated. Marker compounds (matrine, benzoylaconitine, benzoylhypaconitine, benzoylmesaconitine, rhein, prim-o-glycosylcimifugin, β-sitosterol, astragaloside IV, 6-gingerol) R_f values of spot detected were same as the Chun-7 tablet. Aconitine did not detected in Chun-7 tablet due to its highly toxic nature, which is excluded from safe pharmaceutical preparations to prevent health risks and ensure patient safety.

The results of the qualitative TLC method test, comparing test solutions to its standard solutions are presented in Table 5.

Table 5. Identification test results of Chun-7 tablet

Ingredients of Chun-7 tablet	Active compound	Result of marker compounds	Results of Chun-7 tablet
Sophorae flavecens	Matrine	R_f=0.25±0.03	Sophorae flavencens, Chinese pharmacopoeia 2020
Aconitum kusnezoffii	Aconitine Benzoylaconitine Benzoylhypaconitine Benzoylmesaconitine	R_f=0.85±0.03 R_f=0.63±0.03 R_f=0.56±0.03 R_f=0.54±0.03	Processed Aconite root, Japanese pharmacopoeia, 18
Rheum undulatum	Rhein	R_f=0.25±0.03	Rhei radix, Chinese pharmacopoeia, 2020
Saposhnikovia divaricata	Prim-O-glucosylcimifugin	R_f=0.36±0.03	Saposhnikoviae radix, Chinese pharmacopoeia, 2020
Glehnia littoralis	β-sitosterol	R_f=0.69±0.03	Typhonii rhizome, Chinese pharmacopoeia, 2020
Astragalus mongolicus	Astragaloside IV	R_f=0.71±0.03	Astragalus root, Japanese pharmacopoeia, 18
Zingiberis officinale	6-gingerol	R_f=0.70±0.03	Zingiberis rhizome recens, Chinese pharmacopoeia, 2020

Total content of alkaloids and phenolic compounds in Chun-7 tablet were examined to be 1.2 mg, 8 mg in per tablet, respectively as shown in Table 6.

Table 6. Results of total alkaloids and phenolic content in Chun-7

Formulation	Total alkaloids (mg per tablet)	Total phenolic content (mg per tablet)
Chun-7 tablet	1.2	8

Matrine was selected as the marker compound to establish the calibration curve due to its well-characterized chemical properties and its reliable quantification in alkaloid content analysis, particularly with the bromocresol green method. Gallic acid was used as the marker compound in the Folin-Ciocalteu method due to its well-established reactivity with the reagent, reliable absorbance properties, and its widespread use as a standard for phenolic quantification. The results of the validation of analytical procedures are presented in Table 7.

Table 7. Result of parameters obtained from method validation.

Parameters	Matrine	Gallic acid
Concentration limit (μg/mL)	1-6	51.25-205
Correlation coefficient (r^2)	1.0000	0.9966
Slope	0.0455	4.5531
Intercept	0.0009	0.0199
Standard error (intercept)	0.0130	0.0188
Standard deviation (intercept)	0.0790	0.2517
LOD (μg/mL)	1.02	14.4
LOQ (μg/mL)	3.08	43.6

The standard matrine and gallic acid solution concentration limits were 1-6 μg/mL and 51.25-205 μg/mL, respectively. The standard matrine solution's detection limit was 1.02 μg/mL, and the limit of quantification was 3.08 μg/mL. The standard gallic acid solution's detection limit was 14.4 μg/mL, and the limit of quantification was 43.6 μg/mL. The standard marine and gallic acid correlation coefficients were 1 and 0.9966, respectively, showing that analytical methods are qualified.

Microbial contamination

The Chun-7 tablet's microbial contamination results and requirements are presented in Table 8.

Table 8. Microbial contamination results of Chun-7 tablet.

№	Parameters	Requirements	Results
1	Total aerobic microbial count	Not more than 10^5 cfu/g	$1x10^4$ cfu/g
2	Total yeast and mold count	Not more than 10^4 cfu/g	$1x10^3$ cfu/g
3	Bile-tolerant gram-negative bacteria counts	Not more than 10^4 cfu/g	$<10^1$ cfu/g
4	*Escherichia coli*	Absent	Absent
5	*Salmonella*	Absent	Absent

Total aerobic microbial count was $1x10^4$ cfu/g, total yeast and mold count was $1x10^3$ cfu/g, bile-tolerant gram-negative bacteria count was not more than 10 cfu/g, and *Salmonella, Escherichia coli* were absent, which were admitted to acceptable limits as prescribed in requirements.

DISCUSSION

The formulation and evaluation of Chun-7 herbal tablets in this study are significant in traditional herbal medicine transitioning into modern pharmaceutical forms. The successful development of these tablets addresses common challenges associated with herbal powders, such as dosing precision and patient compliance. Comparable research has demonstrated similar efforts in transforming traditional herbal formulations into tablet forms to enhance their practicality and effectiveness.

For instance, Monton et al. (2014) investigated the formulation and physical properties of fast-disintegrating tablets derived from a traditional Thai formula. They employed wet granulation techniques similar to those used in this study, highlighting the efficacy of ethanol as a binder to improve granule cohesion and tablet integrity. Their findings, which revealed acceptable hardness and friability values, align with the results obtained for the Chun-7 tablets, thus validating the use of ethanol in herbal tablet formulations.[22]

Similarly, the formulation of Ayurvedic herbal tablets has been explored, demonstrating the importance of optimizing moisture content during granulation to achieve desired tablet characteristics. Studies on Ayurvedic formulations such as Triphala have shown that precise control over granule moisture levels can significantly impact tablet hardness and disintegration time, ensuring the release of active ingredients in a controlled manner.[23] This resonates with our findings, where 5% and 6% moisture content tablets exhibited optimal hardness and acceptable friability.

Sophorae flavescens, main ingredient of Chun-7 tablet, contains relatable amounts of matrine and oxymatrine. These compounds are members of the quinolizidine alkaloid class, known to exhibit anticolitis, antifibrosis, anti-inflammatory, antiviral effects.[24] Polyphenols have high molecular weight and high concentration in most

plants. The non-flavonoid phenolic compounds have antioxidant activity as chelators and free radical scavengers,, with a remarkable impact on peroxyl, hydroxyl radicals, and peroxynitrites.

One of the typical non-flavonoid phenolic compounds representative is gallic acid.

Chinese traditional medicine Lianhua Qingwen capsule is well known as a novel treatment for COVID-19. A qualitative analysis of the Lianhua Qingwen capsule identified 104 compounds, such as alkaloids, flavonoids, phenols, phenolic acids, phenylpropanoids, quinones, terpenoids, and other phytochemicals.[25] In our study, we identified ten compounds, which are primary active ingredients, such as alkaloids, phenols, anthraquinones, glycosides, and steroids. Both the Lianhua Qingwen capsule and Chun-7 tablet contain alkaloids and phenolics, which have moderate effects on viral lung disease. In another perspective, Chun-7 tablets contain various herbal ingredients; they are convenient for determining the overall compounds, such as total alkaloids and phenolic compounds. We selected and validated UV-Vis spectrophotometric methods for total alkaloids and phenolics, which are suitable for standardizing the finished product These studies consistently highlight the importance of maintaining stringent quality control measures during the tablet formulation process, similar to the approach taken in this research.

CONCLUSION

The formulation and evaluation of Chun-7 antiviral herbal tablets demonstrated promising results in terms of physical and mechanical properties. The prepared tablets exhibited acceptable weight variation, hardness, and friability, aligning with established standards. Specifically, tablets compressed with 5% and 6% granule moisture content showed optimal hardness and friability, indicating their suitability for practical use. The study highlights the wet granulation method's effectiveness and moisture content's impact on tablet characteristics. Therefore, qualitative and quantitative analyses were performed in tablets with granules at 6% moisture. The results of qualification and quantification of the Chun-7 tablet met the requirements according to MNP. Overall, the Chun-7 tablets offer a viable alternative to traditional powder formulations, enhancing convenience and efficacy

in administering herbal medicines for respiratory tract infections. Further research is recommended to explore the clinical efficacy and stability testing for the Chun-7 tablet.

REFERENCES

1. van Doorn HR, Yu H. Viral Respiratory Infections. In: Ryan ET, Hill DR, Solomon T, Aronson NE, Endy TP, eds. Hunter's Tropical Medicine and Emerging Infectious Diseases. 10th ed. Elsevier; 2020:284-288. doi:10.1016/B978-0-323-55512-8.00033-8.
2. Yang YF, Liu TT, Li GX, Chen XQ, Li RT, Zhang ZJ. Flavonoids from the Roots of Sophora flavescens and Their Potential Anti-Inflammatory and Antiproliferative Activities. Molecules. 2023;28(5):2048. DOI: 10.3390/molecules28052048.
3. He X, Fang J, Huang L, Wang J, Huang X. Sophora flavescens Ait.: Traditional usage, phytochemistry and pharmacology of an important traditional Chinese medicine. J Ethnopharmacol. 2015;172:10-29. DOI: 10.1016/j.jep.2015.06.010.
4. Kolodziejczyk-Czepas J, Liudvytska O. Rheum rhaponticum and Rheum rhabarbarum: a review of phytochemistry, biological activities and therapeutic potential. Phytochem Rev. 2021;20:589-607. DOI: 10.1007/s11101-020-09715-3.
5. Yang M, Li X, Zhang L, et al. Ethnopharmacology, Phytochemistry, and Pharmacology of the Genus Glehnia: A Systematic Review. Evid Based Complement Alternat Med. 2019; 2019:1253493. DOI: 10.1155/2019/1253493.
6. Yang M, Wang CC, Wang WL, et al. Saposhnikovia divaricata—An Ethnopharmacological, Phytochemical and Pharmacological Review. Chin J Integr Med. 2020;26:873-880. DOI: 10.1007/s11655-020-3091-x.
7. Gong F, Qu R, Li Y, Lv Y, Dai J. Astragalus Mongholicus: A review of its anti-fibrosis properties. Front Pharmacol. 2022;13:976561. DOI: 10.3389/fphar.2022.976561.
8. Yu DH, Bao YM, Wei CL, An LJ. Studies of Chemical Constituents and Their Antioxidant
9. Activities from Astragalus mongholicus Bunge. Biomed Environ Sci. 2005;18:297-301.
10. Shahrajabian MH, Sun W, Cheng Q. Pharmacological Uses and Health Benefits of Ginger (Zingiber officinale) in Traditional Asian and Ancient Chinese Medicine, and Modern Practice. Not Sci Biol. 2019;11(3):309-319. DOI: 10.15835/nsb11310419.
11. Mishra RK, Kumar A, Kumar A. Pharmacological activity of Zingiber officinale. Int J Pharm Chem Sci. 2012;1(3):1073-1078.
12. Fu YP, Zou YF, Lei FY, Wangensteen H, Inngjerdingen KT. Aconitum carmichaelii Debeaux: A systematic review on traditional use, and the chemical structures and pharmacological properties of polysaccharides and phenloc compounds in the roots. J.Ethnopharmacol. 2022:291:115148. DOI: 10.1016/j.jep.2022.115148
13. Shanmugam S. Granulation techniques and technologies: recent progresses. BioImpacts. 2015;5(1):55.
14. Rasenack N, Мьller BW. Dissolution rate enhancement by in situ micronization of poorly water-soluble drugs. Pharm Res. 2002;19(12):1894-900.
15. Gupta A, Mishra AK, Singh AK, Gupta V, Bansal P. Formulation and evaluation of herbal tablet containing methanolic extract of roots of Glycyrrhiza glabra L. Int J Pharm Sci Res. 2017;8(1):230-5.
16. Council of Europe. European Pharmacopoeia. 10th ed. Stasbourg: Council of Europe; 2023. Powder flow. p 387.
17. Mongolian Ministry of Health. Mongolian National Pharmacopeia. 1st ed. Ulaanbaatar: 2011. General specifications for tablets. p 471.
18. Chinese Pharmacopoeia Comission. Pharmacopoeia of the People's Republic of

China. Beijing: China Medical Science Press; 2015.

19. Japanese Pharmacopoeia. Japanese Pharmacopoeia, 18th ed. Tokyo: Pharmaceutical Society of Japan; 2021.
20. Institute of Traditional Medicine and Technology. Mongolian Traditional Medicine Pharmacopoeia, Volume 40, Institute of Traditional Medicine and Technology: 2022. Erdene-7 traditional medicine; p 66-68.
21. International Conference on Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH). Validation of Analytical Procedures: Text and Methodology Q2(R1), 1995.
22. Mongolian Ministry of Health. Ministrial order on Pharmaceutical Regulations. No A/219. 2017.
23. Monton C, Saingam W, Suksaeree J, Sakunpak A, Kraisintu K. Preformulation and physical properties study of fast disintegrating tablets from Thai traditional formula. Int J Pharm Pharm Sci. 2014;6:431-4.
24. Shah B, Seth A, Bhavsar C. Comparative evaluation of marketed herbal formulations of Triphala based on the phytochemical and physicochemical analysis. J Pharmacogn Phytochem. 2016;5(4):48-52.
25. Wang R., Deng X., Gao Q., Wu X., Han L., Gao X., Zhao S., Chen W., Zhou R., Li Z., Bai C. *Sophora alopecuroides* L.: An Ethnopharmacological, Phytochemical, and Pharmacological Review. J.Ethnopharmacol. 2020, 248, 112172 DOI: 10.1016/j.jep.2019.112172.
25. Shuai F., Rongrong Cheng., Zixin Deng., Tiangang Liu., Qualitative analysis of chemical components in Lianhua Qingwen capsule by HPLC-Q Exactive-Orbitrap-MS coupled with GC-MS. Journal of Pharmaceutical Analysis, 2021.