Study Protocol

Study Title

Efficacy and Safety of Cordyceps sinensis Mycelium Culture Extract (Cs4) Supplementation in Pneumoconiosis Rehabilitation: a randomized, controlled trial

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Pending assignment

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Protocol Summary

Title of the project: Efficacy and Safety of Cordyceps sinensis Mycelium Culture Extract (Cs4) Supplementation in Pneumoconiosis Rehabilitation: a randomized, controlled trial

Study Design: Single-center, randomized, double-blind, parallel-group, placebo-controlled, superiority trial.

Population: Adults aged 18–75 years with confirmed pneumoconiosis (diagnosed via chest X-ray/CT and ILO classification).

Intervention: *Cordyceps sinensis* Mycelium Culture Extract (Cs4) 1.6 g/day (0.4 g per capsule, two capsules per dose, twice daily) for 24 weeks.

Control: Matching placebo (starch, sucrose, and colorants) for 24 weeks.

Follow-up: 12 weeks post-intervention (total study duration per participant: 36 weeks).

Primary Outcome: Change in Forced Expiratory Volume in 1 second / Forced Vital Capacity ratio (FEV1/FVC) from baseline to Week 24.

Secondary Outcomes: Change in FEV1, FVC, 6-Minute Walk Test (6MWT) distance, St. George's Respiratory Questionnaire (SGRQ), mMRC Dyspnea Scale, Leicester Cough Questionnaire (LCQ), hs-CRP, IL-6, MDA, SOD, and GPx.

Sample Size: 84 participants (42 per group), accounting for 10% attrition.

Key Inclusion Criteria: Confirmed pneumoconiosis; stable respiratory condition ≥3 months; age 18–75; able to provide informed consent.

Key Exclusion Criteria: Other chronic respiratory diseases (e.g., asthma, COPD); allergy to Cordyceps; pregnancy; severe comorbidities (e.g., active cancer, heart failure); use of investigational product within 30 days.

Abbreviations: 6MWT: 6-Minute Walk Test; ANCOVA: Analysis of Covariance; ATS: American Thoracic Society; CRF: Case Report Form; Cs4: Cordyceps sinensis Mycelium Culture Extract; CTCAE: Common Terminology Criteria for Adverse Events; EDC: Electronic Data Capture; ERS: European Respiratory Society; FEV1: Forced Expiratory Volume in 1 second; FVC: Forced Vital Capacity; GPx: Glutathione Peroxidase; HADS: Hospital Anxiety and Depression Scale; IL-6: Interleukin-6; IPW: Inverse Probability Weighting; IRB: Institutional Review Board; ITT: Intention-To-Treat; LCQ: Leicester Cough Questionnaire; LFT: Liver Function Test; LOCF: Last Observation Carried Forward; MAR: Missing At Random; MCAR: Missing Completely At Random; MDA: Malondialdehyde; MI: Multiple Imputation; MMRM: Mixed Model for Repeated Measures; mMRC: Modified Medical Research Council; PI: Principal Investigator; PP: Per-Protocol; RFT: Renal Function Test; RSD: Relative Standard Deviation; SAE: Serious Adverse Event; SGRQ: St. George's Respiratory Questionnaire; SOD: Superoxide Dismutase; TBARS: Thiobarbituric Acid Reactive Substances; TCM: Traditional Chinese Medicine; UHPLC: Ultra-High Performance Liquid Chromatography; ULN: Upper Limit of Normal;

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Background

Pneumoconiosis is characterized by progressive pulmonary fibrosis resulting from prolonged inhalation and retention of pathogenic mineral dusts (e.g., silica, coal, asbestos) in a series of occupational interstitial lung diseases (1-3). Clinically, it manifests as chronic cough, sputum production, dyspnoea, and chest pain, with morbidity and mortality rates directly correlated to dust exposure duration and pathogenicity. Epidemiological data underscore its growing public health burden. According to reports from the National Institute of Occupational Safety and Health, there has been a marked increase in incidence since the early 21st century (4, 5), with over 870,000 cases and a mortality rate exceeding 31.2% documented in mainland China (6). The 2018 Chinese Statistical Bulletin on Health and Healthcare Development identified pneumoconiosis as the predominant occupational disease, constituting 82.85% (19,468/23,497) of reported occupational illnesses (7). Silicosis was the most prevalent subtype, contributing a 12.7% prevalence among high-risk workers from 2002 to 2016 (8). Beyond its clinical toll, pneumoconiosis imposes substantial socioeconomic costs, with estimated annual economic losses in China surpassing 184.5 billion RMB due to healthcare expenditures, lost productivity, and disability compensation (9).

Current therapeutic strategies, including whole lung lavage, lung transplantation, and experimental stem cell therapies, remain limited by procedural invasiveness, exorbitant costs, and restrictive eligibility criteria (10, 11). These limitations highlight an urgent need for cost-effective, scalable interventions. Traditional Chinese Medicine (TCM) has garnered attention as a complementary approach, with preliminary studies demonstrating improvements in pulmonary function, symptom management (e.g., reduced dyspnea, enhanced exercise tolerance), and quality- of-life metrics in pneumoconiosis patients (12, 13). The holistic framework of TCM aligns with the multifactorial pathophysiology of pneumoconiosis by targeting immune modulation, anti- fibrotic pathways, and systemic homeostasis. However, existing evidence is constrained by methodological shortcomings, including small sample sizes, non-randomized designs, and insufficient blinding, which preclude definitive conclusions regarding efficacy (12, 13).

Cordyceps sinensis (Dong-Cong-Xia-Cao) is a well-known Chinese herbal medicine known for its tonifying properties and ability to address deficiency syndromes according to Chinese medicine principles. It is widely believed that Cordyceps supplementation can enhance overall health, particularly for individuals with chronic and severe lung illnesses. Due to its rarity, long-term use of Cordyceps sinensis is often unaffordable for most people. However, its standardized fermentation product, Cordyceps sinensis Mycelium Culture Extract (Cs4), is now widely accepted as a more affordable alternative due to its similar chemical composition to wild Cordyceps sinensis. Pre-clinical investigations revealed that Cordyceps Cs4 possessed anti-inflammatory, anti-tumor, and immunomodulatory effects, as well as regulation of glucose and energy metabolism (14-18). Pneumoconiosis is classified in TCM as "Lung Bi" (肺痺), characterized by the invasion of pathogenic dust (塵毒) into the lung, leading to Qi stagnation, Blood stasis, and accumulation of Phlegm-turbidity. Prolonged retention of these pathogenic factors depletes Lung Qi and Kidney Qi, ultimately resulting in pulmonary fibrosis — a manifestation of deficiency of Zheng Qi (正氣虧虛) coupled with excess of pathogenic retention. According to TCM theory, Cordyceps sinensis is classified as a Kidney-tonifying and Lung-nourishing drug. It acts on the Lung and Kidney meridians, replenishing Essence and Qi, thereby addressing the root deficiency (本虛) underlying pneumoconiosis. Its ability to simultaneously tonify and astringe makes it particularly suitable for chronic deficiency syndromes associated with occupational lung diseases.

Pre- clinical studies revealed that in a rodent model of upper-respiratory diseases, Cordyceps or Cs4 can improve immune hypersensitivity reactions, reduce inflammation, and

delay lung fibrosis (18, 19). A randomized trial showed that Cordyceps treatment can improve pulmonary function in asthma patients ($z=2.442$, $p=0.015$ in FEV1, $z=2.162$, $p=0.031$in FEV1/FVC) (20), indicating its potential therapeutic effect of improving pulmonary function in patients with wider types of lung diseases.

In our preliminary study, we recruited 110 patients with some of the common manifestations of long-COVID, including dyspnea, fatigue, headache, cough, chest pain, and joint pain. Patients were randomized into intervention and waitlist-controlled arms (Figure 1 in the Preliminary Data section) and followed up for a 3-month oral intake of Cordyceps Cs4 daily at the dose of 1.6g (0.4g per capsule, 2 capsules per time, twice per day). The baseline characteristics of the two groups are shown in Table 1 in the Preliminary Data section. Health conditions of patients were assessed by the Score of Insomnia Severity Index (ISI), Brief Fatigue Inventory Form (BFI), St. George's Respiratory Questionnaire (SGRQ), Hospital Anxiety and Depression Scale (HADS), and Short Form 12 (SF12). Our pilot findings revealed that compared to waitlist-controlled arm, 3-month Cs4 intervention arm exhibited significant improvement in fatigue inventory (39.00 (19.00-46.50) v.s. 46.00 (33.00- 61.00) in median (IQR), intervention v.s. waitlist-controlled, $p<0.05$), insomnia severity index (10.00 (7.00-13.50) v.s. 13.00 (11.00-17.50), $p<0.05$), respiratory symptoms (22.06 (12.13-27.26) v.s. 34.72 (29.12-43.27), $p<0.05$), physical score (45.59 (40.78-50.94) v.s. 38.99 (34.76-45.11, $p<0.05$) and mental score (48.66 (44.30-53.25) v.s. 42.34 (35.54-52.03), $p<0.05$), while showed no potent effect on depression (6.00 (2.50-8.00) v.s. 8.00 (5.00-9.00), $p>0.05$) and anxiety (7.00 (4.50-9.00) v.s. 8.00 (5.00-9.00), $p>0.05$) of the patients (Table 2 in Annex I Preliminary Data). Notably, in the St. George's Respiratory Questionnaire (SGRQ), patients self-declared significant improvement in the function, activity, and impact of the respiratory system after Cs4 treatment. This prompts us to consider the therapeutic potential of Cs4 in rehabilitating lung function in patients with pneumoconiosis.

Objectives

To investigate the efficacy and safety of Cordyceps sinensis Mycelium Culture Extract (Cs4) supplementation on lung function rehabilitation in pneumoconiosis patients, and its clinical association with multiple factors such as exercise capacity, quality of life, inflammation, and oxidative stress.

Hypothesis

Compared to placebo, 24 weeks of daily Cs4 supplementation leads to a significantly greater improvement in lung function (FEV1 and FVC) in adults with pneumoconiosis.

Trial Design

This is a single-center, randomized, double-blind, parallel-group, placebo-controlled trial conducted at the School of Chinese Medicine, The University of Hong Kong.

Subject recruitment:

Recruitment will be conducted through clinic referrals, advertisements in local newspapers, and online platforms. Interested participants will undergo an in-person screening visit to the clinic of the School of Chinese Medicine, The University of Hong Kong.

Sample Size Calculation

Based on our pilot study on the FEV1/FVC ratio data (Treatment: 0.74±0.08, n=30; Control: 0.69±0.07, n=26), we assumed a between-group difference of 0.05 (5 percentage points) in FEV1/FVC with a pooled standard deviation of 0.078, corresponding to a standardized mean difference (Cohen's d) of 0.64. Using a two-sided α of 0.05 and exactly 80% power, 38 participants per group are required for the primary analysis. To account for an anticipated 10% attrition rate, we plan to recruit 42 participants per group (total n=84).

Randomization

After screening and baseline assessments, eligible participants will be randomly assigned to the Cs4 intervention group or the placebo control group at a ratio of 1:1, with stratification on the level of pneumoconiosis. The random sequences generated in R statistical package will have a block of 4 in each cycle, consisting of two control groups and two intervention groups. Assignments will be sealed in opaque envelopes and opened only after eligibility is confirmed and consent is obtained.

Blinding Process

The randomization code will be held by an independent third party not involved in study conduct or analysis. The research study personnel involved in recruiting and screening participants, as well as those enrolled in the study and assessors conducting baseline and follow-up evaluations, will be blinded to the treatment allocation. In case of an emergency requiring unblinding (e.g., serious adverse event), the investigator may request code breaking through the designated unblinding procedure. Emergency unblinding envelopes will be available at the trial site. The date, time, reason, and personnel involved in unblinding will be documented.

Inclusion Criteria

Participants must meet ALL of the following criteria:

1. Adults aged 18–75 years;

2. Diagnosed with pneumoconiosis based on clinical and radiological criteria (chest X-ray/CT and ILO classification);

3. Stable respiratory condition for at least 3 months prior to enrollment (no acute exacerbations, hospitalizations, or changes in respiratory medication);

4. Able to provide written informed consent.

Exclusion Criteria

Participants meeting ANY of the following criteria will be excluded:

1. History of chronic respiratory diseases other than pneumoconiosis that may confound FEV_1/FVC assessment (e.g., asthma, bronchiectasis, and interstitial lung disease of other etiologies).
2. Known allergy to *Cordyceps sinensis* or any component of the supplement.
3. Pregnant or breastfeeding women.
4. Severe comorbid conditions that could interfere with participation (e.g., active cancer, decompensated heart failure [NYHA Class III–IV], uncontrolled psychiatric illness).

Withdrawal Criteria

Participants may withdraw from the study if they:

1. Withdraw consent at any time without prejudice.
2. Develop a serious adverse event (SAE) requiring discontinuation of the investigational product, as determined by the PI or Safety monitoring committee.
3. Experience intolerable adverse events.
4. Develop an exclusion criterion during the study (e.g., pregnancy, new malignancy).
5. Are lost to follow-up after reasonable attempts to contact (minimum 3 attempts via telephone and email).

Intervention

The investigational product is Cordyceps sinensis Mycelium Culture Extract (Cs4), administered orally at a dose of 1.6 g per day (0.4 g per capsule, two capsules per dose, twice daily) for a duration of 24 weeks. The capsules will be packaged in blister packs that are identical in appearance to the placebo. Participants who are taking any herbal supplement at screening will undergo a 2-week washout period before baseline assessments and randomization. The placebo will consist of starch, sucrose, and food-grade colorants, and will be identical to the Cs4 capsules in size, color, weight, and smell, packaged in identical blister packs to maintain blinding.

Compliance will be monitored through multiple measures. Participants will maintain a daily intake record form, and pill count will be performed at each visit (Week 2, Month 3, Month 6, and Month 9). Any unused capsules will be returned and counted at each visit to assess adherence.

The quality of tested samples will be measured and controlled by determining (a) the UHPLC-chromatographic fingerprint of Cs4 according to literature report (21) and (b) the content of adenosine by UHPLC according to China Pharmacopeia (Ed2020) 0-, 1-, 2-, 4-, 6-,

12- and 24-month after receiving the tested samples. The similarity of UHPLC fingerprint should be more than 96% while adenosine should be more than 0.010% with RSD<10% among batches of Cs4 capsules. The placebo capsule contain starch, sucrose and colorants, which will have similar characteristics to the research capsule. Drug compliance will be monitored at each visit, with good drug compliance defined as taking more than 80% of the prescribed pill count.

Outcome Measures

(a) **Primary Outcome**

Change in Forced Expiratory Volume in 1 second (FEV1) and Forced Vital Capacity (FVC) from baseline to Month 6 (Week 24), measured by spirometry conducted according to ATS/ERS guidelines.

(b) **Secondary Outcomes**

1. Lung Function: Change in FEV1 (L) and FVC (L) from baseline to Month 3 and 9.
2. Exercise Capacity: Change in 6MWT distance (meters) from baseline to Month 3, 6, and 9.
3. Quality of Life: Change in SGRQ total and component scores (Symptoms, Activity, Impacts) from baseline to Month 3, 6, and 9.
4. Symptom Burden: Change in mMRC Dyspnea Scale and LCQ scores from baseline to Month 3, 6, and 9.
5. Inflammation: Change in hs-CRP and IL-6 levels from baseline to Month 6 and 9.
6. Oxidative Stress: Change in MDA, SOD, and GPx levels from baseline to Month 6 and 9.

(c) **Safety Outcomes**

1. Adverse events (AEs): Any untoward medical occurrence during the 2-week screening, 24-week intervention, and 12-week follow-up, graded by CTCAE v5.0 (Grades 1–5). Causality assessed by the PI as unrelated, unlikely, possible, probable, or definite.
2. Serious adverse events (SAEs): Death, life-threatening events, hospitalization, disability, or other important medical events. Reported to the PI within 24 hours and to the IRB within 5 working days.
3. Safety assessments: Adverse event monitoring at baseline, Week 2, Month 3, Month 6, and Month 9; safety blood tests (CBC, LFT, RFT) at Week 2 (±5 days), Month 6, and Month 9.

(d) **Exploratory Outcomes**

1. Inflammatory markers: Blood samples collected at baseline, Month 6, and Month 9. hs-CRP measured by immunoturbidimetric assay; IL-6 measured by high-sensitivity ELISA.
2. Oxidative stress markers: Blood samples collected at baseline, Month 6, and Month 9. MDA by TBARS assay; SOD activity by colorimetric assay (NBT reduction); GPx activity by coupled enzyme assay (NADPH oxidation).
3. Symptom scores: mMRC Dyspnea Scale (grades 0–4) and LCQ (19 items across physical, psychological, and social domains; higher scores indicate better quality of life) administered at baseline, Months 3, 6, and 9.

Outcome Measurement Schedule

Outcome Measure	Baseline	Week 2	Month 3	Month 6	Month 9
Primary Outcomes					
Lung function parameters (FEV1, FVC)	✓			✓	
Secondary Outcomes					
Lung function parameters (FEV1, FVC)	✓		✓		✓
6-minute walk test (6MWT)	✓		✓	✓	✓
St. George's Respiratory Questionnaire (SGRQ)	✓		✓	✓	✓
Exploratory Outcomes					
Inflammatory markers (hs-CRP, IL-6)	✓			✓	✓
Oxidative stress markers (MDA, SOD, GPx)	✓			✓	✓
mMRC Dyspnea Scale	✓		✓	✓	✓
Leicester Cough Questionnaire (LCQ)	✓		✓	✓	✓
Safety Outcomes					
Safety blood test (CBC, liver/renal function)	✓	✓		✓	✓
Adverse events monitoring	✓	✓	✓	✓	✓

Data Collection and Management

(a) Data Collection:

All data will be collected by trained study personnel. Data will be recorded on standardized case report forms (CRFs). Research Electronic Data Capture systems (REDCap) will be used to ensure data accuracy and facilitate data management. Data from spirometry, 6MWT, blood tests, and questionnaires will be entered into the EDC system by designated data entry personnel.

(b) Baseline and confounding factors analysis:

Baseline characteristics will be collected for age, gender, race, job, educational background, height, body weight, blood pressure, other comorbidities, and blood test on whole blood cells.

(c) Efficacy and safety analysis:

Intention-to-treatment approach will be used for data analysis. For participants lost to follow-up or drop-out, inverse probability weighting (IPW) will be used to deal with the missing data

and potential selection bias. The generalized linear regression model will be used to determine the efficacy of Cs4 at 6-months and 9-months. Age, gender, baseline BMI, job, educational background, sleep quality will be used as covariates in the regression model to control confounding factors. Subgroup analysis will be conducted in gender and age category. Sensitivity analysis will be conducted including per-protocol dataset analysis, multiple imputation and adjustment for attendance rate. Results will be presented as mean differences between groups with 95% confidence intervals. We considered a two-sided P value <0.05 to indicate statistical significance. All data processing and analysis will be conducted in R statistical software (Version 4.3).

(d) Data handling

All personal and study data will be managed throughout the study period by authorized study personnel. Access to personal and study data during and after the study will be restricted to the Principal Investigator, Co-investigator, and Data Manager. Access will be controlled through a password-protected electronic system (REDCap) and secure physical storage.

Raw data, including signed informed consent forms, source documents, case report forms, and laboratory reports, will be stored in a locked cabinet within a secure room with limited access at the trial site. Data entry will be performed exclusively on password-protected computers accessible only to authorized personnel. The Principal Investigator and Data Manager will be responsible for the safekeeping of all personal and study data during and after the study. The Principal Investigator will retain ultimate responsibility for oversight of data confidentiality, integrity, and security.

Upon study completion, all personal and study data will be preserved for a period of five years, after which they will be securely disposed of, unless an application for extended retention is approved by the Institutional Review Board. Prior to any statistical analysis, all personal identifying information will be removed from the dataset; each participant will be assigned a unique study identifier, and the master linkage file connecting identifiers to personal identities will be stored separately in an encrypted format accessible only to the Principal Investigator.

Participant Compensation and Post-Trial Care

A travel reimbursement of up to HKD 400 will be provided after participants have finished all follow-ups. Participants will be covered by clinical trial insurance for any physical injury directly resulting from study participation, and in the event of a study-related injury, necessary medical treatment will be provided free of charge with compensation available according to the insurance policy terms. As the study product is commercially available, the study team will not provide further supply after trial completion. Participants requiring ongoing treatment will be transitioned to standard care with referral to their attending physician, and participants will be responsible for associated costs. Treatment allocation will be disclosed to participants upon study completion upon request.

Ethics and Regulatory Considerations

This protocol, the informed consent form, and all participant-facing materials will be submitted to the HKU/HA HKW Institutional Review Board (IRB) for approval before any study procedures commence, and no participant will be enrolled before written IRB approval is obtained.

Written informed consent will be obtained by the Principal Investigator or a delegated, GCP-trained study physician or research assistant. The consent process will be conducted in the participant's preferred language (Cantonese, Mandarin, or English), and participants will be given as much time as they need to consider participation. A copy of the signed consent form will be provided to the participant. Participants with limited literacy will be provided with verbal explanation and witnessed consent. Non-Chinese participants will be offered interpreter services. Participants with cognitive impairment affecting decision-making capacity will be excluded.

Statement of Compliance

This trial will be conducted in compliance with this protocol, the principles of Good Clinical Practice as outlined in ICH E6(R2), and the Declaration of Helsinki. The protocol follows the SPIRIT 2013 Statement, and trial outcomes will be reported in compliance with the CONSORT 2010 Statement.

Funding

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References

1. Hou X, Wei Z, Jiang X, Wei C, Dong L, Li Y, et al. A comprehensive retrospect on the current perspectives and future prospects of pneumoconiosis. Front Public Health. 2024;12:1435840.
2. Berardi R, Balestri P, Tomaccini D, Borgogni P, Mattei R. [Empty sella syndrome: a cause of GH deficiency?]. Pediatr Med Chir. 1982;4(4):393-4.
3. Vanka KS, Shukla S, Gomez HM, James C, Palanisami T, Williams K, et al. Understanding the pathogenesis of occupational coal and silica dust-associated lung disease. Eur Respir Rev. 2022;31(165).
4. Leonard R, Zulfikar R, Stansbury R. Coal mining and lung disease in the 21st century. Curr Opin Pulm Med. 2020;26(2):135-41.
5. Blackley DJ, Halldin CN, Laney AS. Continued Increase in Prevalence of Coal Workers' Pneumoconiosis in the United States, 1970-2017. Am J Public Health. 2018;108(9):1220-2.
6. Li J, Yin P, Wang H, Wang L, You J, Liu J, et al. The burden of pneumoconiosis in China: an analysis from the Global Burden of Disease Study 2019. BMC Public Health. 2022;22(1):1114.
7. Hu W, Wu WN, Qiao Q. Occupational survey-based evidence of health status and welfare problems of workers with pneumoconiosis in China. Front Public Health. 2023;11:1142161.
8. Hoy RF, Dimitriadis C, Abramson M, Glass DC, Gwini S, Hore-Lacy F, et al. Prevalence and risk factors for silicosis among a large cohort of stone benchtop industry workers. Occup Environ Med. 2023;80(8):439-46.
9. Liang YX, Wong O, Fu H, Hu TX, Xue SZ. The economic burden of pneumoconiosis

in China. Occup Environ Med. 2003;60(6):383-4.
10. Mao WJ, Chen JY, Zheng MF, Ye SG, Liu F, He YJ, et al. Lung transplantation for end-stage silicosis. J Occup Environ Med. 2011;53(8):845-9.
11. Spitalieri P, Quitadamo MC, Orlandi A, Guerra L, Giardina E, Casavola V, et al. Rescue of murine silica-induced lung injury and fibrosis by human embryonic stem cells. Eur Respir J. 2012;39(2):446-57.
12. Li J, Zhao H, Xie Y, Li J, Li Q, Chen X, et al. Clinical efficacy of comprehensive therapy based on traditional Chinese medicine patterns on patients with pneumoconiosis: a pilot double- blind, randomized, and placebo-controlled study. Front Med. 2022;16(5):736-44.
13. Song PP, Liu J, Xiao H, Ma XY, Zhang SQ, Chen YX. [Clinical study on traditional Chinese medicine syndrome differentiation and treatment of pneumoconiosis]. Zhonghua Lao Dong Wei Sheng Zhi Ye Bing Za Zhi. 2019;37(3):186-8.
14. Dai G, Bao T, Xu C, Cooper R, Zhu JS. CordyMax Cs-4 improves steady-state bioenergy status in mouse liver. J Altern Complement Med. 2001;7(3):231-40.
15. Zhao CS, Yin WT, Wang JY, Zhang Y, Yu H, Cooper R, et al. CordyMax Cs-4 improves glucose metabolism and increases insulin sensitivity in normal rats. J Altern Complement Med. 2002;8(3):309-14.
16. Tang J, Tian D, Liu G. Immunosuppressive effect of Cordyceps CS-4 on human monocyte- derived dendritic cells in vitro. Am J Chin Med. 2010;38(5):961-72.
17. Sang Q, Pan Y, Jiang Z, Wang Y, Zhang H, Hu P. HPLC determination of massoia lactone in fermented Cordyceps sinensis mycelium Cs-4 and its anticancer activity in vitro. J Food Biochem. 2020;44(9):e13336.
18. Chen J, Chan WM, Leung HY, Leong PK, Yan CTM, Ko KM. Anti-Inflammatory Effects of a Cordyceps sinensis Mycelium Culture Extract (Cs-4) on Rodent Models of Allergic Rhinitis and Asthma. Molecules. 2020;25(18).
19. Chen M, Cheung FW, Chan MH, Hui PK, Ip SP, Ling YH, et al. Protective roles of Cordyceps on lung fibrosis in cellular and rat models. J Ethnopharmacol. 2012;143(2):448-54.
20. Wang N, Li J, Huang X, Chen W, Chen Y. Herbal Medicine Cordyceps sinensis Improves Health-Related Quality of Life in Moderate-to-Severe Asthma. Evid Based Complement Alternat Med. 2016;2016:6134593.
21. Cao W, Hong L, Yang M, Li S, Zhao J. [Fingerprint establishment and multi-indicator quantitative analysis of fermented Cordyceps powder and products]. Se Pu. 2021;39(9):1006-11.
22. Bellary S, Krishnankutty B, Latha MS. Basics of case report form designing in clinical research. Perspect Clin Res. 2014;5(4):159-66.