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Guben Kechuan Granules for Chronic Bronchitis: A Multicenter, Randomized, Controlled Trial Evaluating Efficacy and Safety

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ABSTRACT

Chronic bronchitis (CB) is a long-standing inflammatory airway disorder with a high global burden and limited treatment success. In recent years, the combined use of traditional Chinese medicine (TCM) with standard medical care has been increasingly adopted for CB and has shown encouraging therapeutic potential. A multicenter randomized controlled trial directed by the China–Japan Friendship Hospital (Beijing, China) recruited 300 individuals with CB aged 18–75 years. Participants were allocated in a 2:2:1 ratio to one of three groups: Guben Kechuan Granules (test group, n=120), Guilong Kechuanning Capsules (active comparator, n=120), or a subject-education arm (blank control, n=60). The intervention lasted 24 weeks, followed by a 24-week observation phase. Efficacy assessments included clinical symptoms, acute exacerbation of CB (AECB), pulmonary function metrics, immune-related indicators, and quality-of-life measurements. Adverse events were recorded for safety analysis. All statistical evaluations were performed with SAS 9.4.

Among the study population, 299 patients (99.7%) were part of the full analysis set, 298 were eligible for safety monitoring, and 278 met criteria for the per-protocol dataset. Relative to the blank control, Guben Kechuan Granules markedly extended the time to first AECB and lowered AECB duration, intensity, and frequency (all $p<0.05$). After 24 weeks, notable reductions were observed in cough scores (−21.85±19.73), sputum scores (−22.74±18.66), and wheezing scores (−21.33±18.76) ($p<0.05$), and these improvements persisted throughout the 24-week follow-up ($p<0.05$). Significant gains in mobility, self-care, daily function, and overall health were also recorded (all $p<0.05$). No meaningful changes in FEV1/FVC%, FEV1%pred, PEF, MMEF, FVC, or FEV1 were detected in any group after 24 weeks. No severe adverse events occurred in the experimental arm during long-term follow-up. Guben Kechuan Granules provided clear therapeutic benefit and exhibited good tolerability in patients with CB, improving symptoms, reducing AECB occurrence and severity, and enhancing quality of life. Registered on 4 September 2022, ChiCTR2200063321. Traditional Chinese Medicine Inheritance and Innovation "Ten-Hundred-Thousand" Talents Program (Qihuang Program, 2019-QTL-003). Chinese Clinical Trials Registry: https://www.chictr.org.cn/showproj.html?proj=177683.

Keywords: Guben Kechuan Granules, Chronic bronchitis, Clinical efficacy, Safety, Randomized controlled study

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Introduction

Chronic bronchitis (CB) is a long-term inflammatory lung condition defined by recurring cough, persistent mucus production, or wheezing lasting at least three months per year for a minimum of two consecutive years [1]. During exacerbations, sputum becomes thick and difficult to expel, creating airflow obstruction, accelerating functional deterioration of the lungs, and increasing vulnerability to respiratory complications, ultimately raising all-cause mortality [2]. A variety of risk contributors—such as older age [3], cigarette smoking [4], secondhand smoke exposure, biomass burning, dust and pollutant exposure [5, 6], and prior histories of tuberculosis, allergies, or asthma [7]—play roles in CB development. Worldwide, CB prevalence among adults varies between 3% and 6% in many Western populations [8]. Rates are much higher in chronic obstructive pulmonary disease (COPD), where up to 74% are affected [9]. Although global incidence dropped between 1990 and 2019, the absolute number of

CB cases and deaths continues to climb [10]. The World Health Organization estimates that roughly 3.4 million deaths each year result from CB-related complications [10]. As a result, effective management strategies remain essential to reducing morbidity and improving COPD outcomes. Despite medical advancements, CB continues to impose substantial health and socioeconomic burdens, particularly in aging societies, making TCM-based integrative approaches an important area of exploration.

The overarching goals in CB therapy are to reduce symptoms, prevent exacerbations, and slow long-term decline by limiting mucus hypersecretion, controlling airway inflammation, and alleviating chronic cough [11]. Standard treatment may include bronchodilators, corticosteroids, antibiotics, and phosphodiesterase-4 inhibitors, as well as nonpharmacological options such as smoking cessation and pulmonary rehabilitation [12]. However, according to a CHEST Expert Panel Report by Malesker *et al*., currently available therapies—especially for chronic cough—often demonstrate limited effectiveness and rely on evidence of modest quality [13–15]. New interventions, including bronchial rhinoplasty, show early promise but remain experimental [14]. These limitations highlight the need for dependable adjunct or alternative therapeutic strategies that can enhance outcomes for CB patients.

Traditional Chinese Medicine (TCM) views illness as a disturbance involving both physical manifestations and deeper functional imbalances, and therefore treats various stages of disease through an integrated philosophy that differs from Western approaches [15]. Several investigations have indicated that TCM-based formulas can ease the discomfort associated with CB. One study by Dong *et al*. found that Zhisou Powder mitigates inflammation by altering the disordered arachidonic acid metabolism, which appears to underlie part of its benefit in CB [16]. Another preparation, Shui Man Jing, produced from dried aerial portions of Veronica linariifolia subsp. dilatata (Nakai & Kitag). Hong has also been explored as a possible therapeutic option for CB [17]. Researchers further documented that Cordyceps sinensis, a well-recognized herbal material in TCM, may strengthen treatment outcomes and enhance life quality for individuals diagnosed with CB [18].

Guben Kechuan Granules, a compound remedy frequently prescribed in TCM, is used for chronic cough, viscous sputum, and breathlessness linked to deficiencies of the spleen and unstable kidney qi. [19, 20] The product is taken after dissolving it in warm water. Its formulation includes Radix Codonopsis, Rhizoma Atractylodis Macrocephalae, Radix Glycyrrhizae Preparata, Poria cocos, Schisandra chinensis Fructus, Radix Ophiopogonis, and Fructus Psoraleae [21]. Clinicians commonly recommend it to CB patients—particularly those in stable phases—because previous reports show improvements in respiratory function, clinical signs, and inflammatory indicators. In older adults with stable COPD, a 12-week adjunct regimen of Guben Kechuan Granule led to better FEV1, PEF, and FEV1/FVC, along with decreases in Th17 and the Th17/Treg ratio [19]. Other findings suggest it may lessen CB symptoms, adjust immune responses, and reduce inflammation [20]. When administered together with salbutamol aerosol, the granules produced a higher total effectiveness rate (99.3%), increased FEV1, FEV1/FVC, PEF, and MMEF, and lowered concentrations of TNF-α, IL-8, IL-10, and IL-15 during stable COPD. Although clinical investigations are currently evaluating the safety and therapeutic potential of Guben Kechuan Granules [ChiCTR2300078017], there is still a lack of robust data specifically addressing its benefits for CB. This research is therefore designed to assess both its effectiveness and safety through a multi-center randomized controlled trial. For comparison, Guilong Kechuanning Capsule—already supported by evidence for CB—serves as the positive control, while a subject-education-only group functions as the blank control. Its inclusion is justified by its established clinical performance and long-term use. A major distinguishing feature of this study is its 48-week duration, which includes real-world tracking of AECB episodes to better evaluate sustained outcomes.

Materials and Methods

Participant recruitment and study design

This randomized, controlled, multi-site investigation (Chinese Clinical Trial Registry: ChiCTR2200063321), organized by Hangzhou Zhongmei Huadong Pharmaceutical Co., Ltd (Zhejiang, China) and carried out by the China-Japan Friendship Hospital (Beijing, China), was created to examine both the safety and the symptom-improving potential of Guben Kechuan Granules in individuals with chronic bronchitis. The protocol was conducted in accordance with the Declaration of Helsinki, GCP standards, and national regulatory requirements.

Recruitment took place from November 2022 through March 2023 at multiple hospitals in China, including the China-Japan Friendship Hospital, Taiyuan Central Hospital, Ningbo Traditional Chinese Medicine Hospital, People's Hospital of Xiangtan County, Hospital of Sanyuan County, People's Hospital of Xindu District (Xingtai

City), People's Hospital of Yanggu County, People's Hospital of Mengyin County, Longhua County Traditional Chinese Medicine Hospital, and Xiyang Public Hospital.

As shown in **Figure 1**, 300 participants were randomly allocated in a 2:2:1 arrangement: 120 to the Guben Kechuan Granules group, 120 to the Guilong Kechuanning Capsule group, and 60 to the subject-education-only group. One person (ID: 257) in the experimental arm did not take the assigned treatment. Thus, the Full Analysis Set (FAS) included 299 participants, the Safety Set (SS) comprised 298, and 278 individuals met requirements for inclusion in the Per Protocol Set (PPS). The study consisted of a 24-week treatment period with follow-up visits every four weeks, followed by a 24-week observation period also scheduled at four-week intervals.

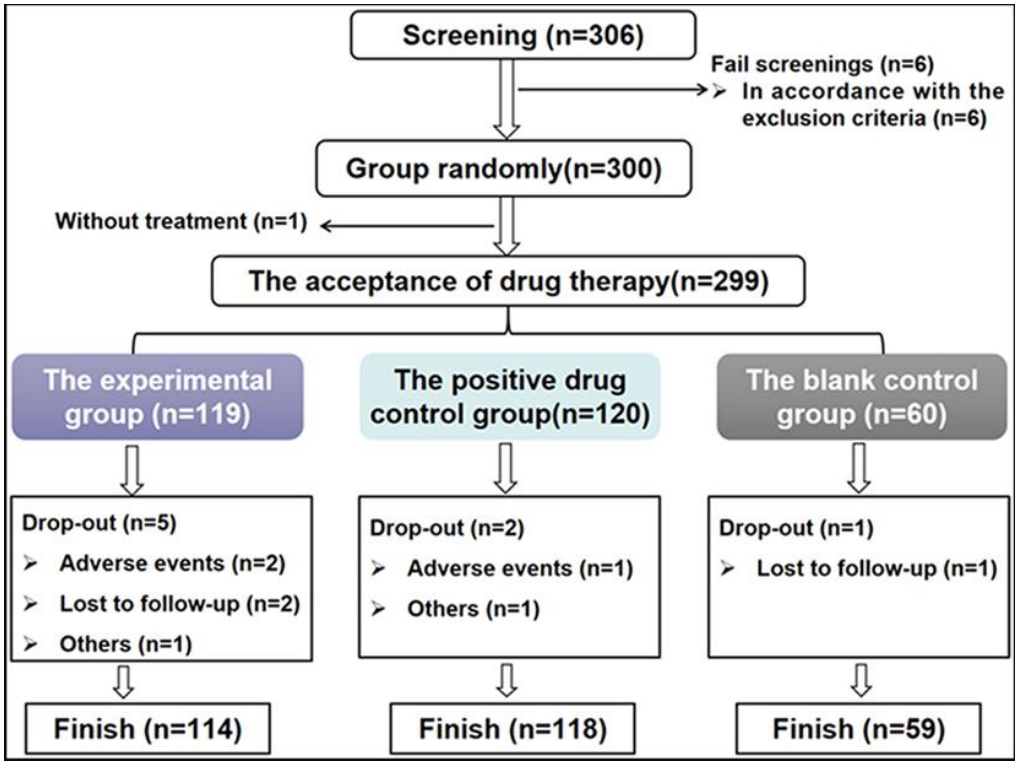

Figure 1. Overview of participant allocation.

Inclusion criteria

Individuals could enter the study only if they fulfilled all of the following:

(1) A confirmed diagnosis of CB, following the standards presented in Internal Medicine (9th edition, 2018, People's Health Publishing House).

(2) Mild clinical manifestations—cough, sputum production, or wheezing—with total symptom ratings ≤ 1.

(3) Age between 18 and 75 years, with no gender restrictions.

(4) Willing participation evidenced by a signed informed consent form.

Exclusion criteria

Participants were not eligible if any of the conditions below applied:

(1) An episode of acute bronchitis or an AECB within the previous month.

(2) Other respiratory illnesses that could mimic CB symptoms, such as pulmonary tuberculosis, eosinophilic bronchitis, bronchogenic carcinoma, idiopathic pulmonary fibrosis, pneumonia, asthma, bronchiectasis, or reflux-related disease.

(3) Intake of medications with similar therapeutic action within the last two weeks.

(4) Impaired hepatic or renal status, including: serum creatinine above the upper reference limit, or ALT and AST values greater than twice the upper normal limit.

(5) Major coexisting diseases affecting the cardiovascular, cerebrovascular, hepatic, renal, gastrointestinal, or hematopoietic systems.

(6) Substance misuse, including prolonged alcohol dependence or drug addiction.

(7) Pregnancy, breastfeeding, or inability to observe strict contraception during the study.

(8) Sensitivity or allergy to any component of the study preparation.
(9) Cognitive impairment or psychiatric illness, including intellectual disabilities or severe mental disorders.
(10) Participation in another clinical study within the last three months.
(11) Any circumstance judged by the investigators to make inclusion unsuitable.

Randomization procedure

A block randomization strategy was applied to maintain even distribution among the groups. After selecting the appropriate block size, a random list for 300 participants was produced using SAS software, assigning them in a 2:2:1 ratio to the experimental arm, the active control arm, or the blank control arm. Each participant received a unique identifier (001–300), linked to their group assignment through a randomization code sheet. Participants were blinded to treatment, and data analysts were also masked. All study medications were placed into uniform containers to minimize recognition.

Medicine interventions

The three study arms received the following regimens:
(1) Experimental group (n = 120): Guben Kechuan Granules, 1 packet (2 g) taken three times per day.
(2) Positive drug group (n = 120): Guilong Kechuanning Capsule, 3 capsules three times daily.
(3) Blank control group (n = 60): Educational guidance only; in the event of AECB, management followed standard clinical protocols.

Use of any additional cough suppressants or expectorants during stable periods was prohibited. Certain therapies were permitted when necessary, including:
(1) Continued treatment for chronic conditions such as diabetes or hypertension.
(2) Interventions required to address adverse events.
(3) Standard management when AECB occurred—antibiotics, antitussives, expectorants, or other medications required for routine care.
(4) TCM decoctions or proprietary Chinese medicines could also be used in AECB, but usage could not exceed 21 consecutive days per episode, with a total duration across the full treatment window limited to three months.

Medication and general procedures

Participants assigned to the Guben Kechuan arm were instructed to take 1 packet (2 g) three times per day, dissolved in warm water prior to ingestion. All subjects—regardless of treatment assignment—received unified education at enrollment and again during follow-up visits.

Assessment of adherence and additional medications

Adherence was summarized using descriptive indicators: number of individuals evaluated, mean values, standard deviations, medians, ranges (minimum to maximum), and the first (Q1) and third (Q3) quartiles. The percentage of adherence was computed using the formula: (amount actually taken / amount expected to be taken) × 100%.

Evaluation of therapeutic benefit and safety

Data on clinical benefit and tolerability were collected during both the intervention phase and the subsequent observation period. The evaluation framework included:

1. Symptom scoring for cough, sputum production, and dyspnea on a 0–100 scale.
2. AECB classification, based on the predefined criteria.
3. Pulmonary function metrics—FEV1, FVC, FEV1% predicted (FEV1%pred), FEV1/FVC, MMEF, and PEF—were measured using the MasterScreen PFT system (Jaeger, Germany).
4. Immune profile testing (CD4+, CD8+, CD4+/CD8+) is available only in centers equipped for immunologic assays.
5. Quality-of-life domains, including mobility, self-maintenance, routine tasks, bodily discomfort, and psychological status (anxiety/depression).

All adverse events were recorded and categorized using System Organ Class (SOC) and Preferred Term (PT) terminology from the most recent MedDRA edition [22].

Statistical strategy

Previous literature reported effective rates of 96.15% for the investigational therapy, 95.00% for the active comparator, and 77.08% for the untreated control [20, 23]. With an anticipated 20% attrition, the minimum sample requirements were projected as 84, 84, and 42 for the corresponding groups. The 20% assumption was based on earlier chronic bronchitis trials of comparable length, though actual attrition reached only 0.33%. Power was fixed at 80% ($\beta = 0.20$) with a two-sided α of 0.05. Analyses were performed in SAS 9.4. Full analysis set (FAS) and per-protocol set (PPS) were used for baseline comparisons, adherence evaluation, and concomitant medication assessment; safety conclusions were derived from the safety set (SS). Continuous variables were summarized using case counts, means, medians, standard deviations, and observed ranges. Categorical results were reported as frequencies and percentages. Group differences were tested using ANOVA or the Kruskal–Wallis H test, and within-group changes were examined using paired t-tests or Wilcoxon signed-rank tests. All p-values were two-tailed, and $p < 0.05$ denoted significance.

Results and Discussion

Demographic and baseline characteristics

Table 1 presents an overview of participant demographics and initial clinical status for the three study cohorts: the experimental arm (n = 119), the active drug comparison arm (n = 120), and the blank control arm (n = 60). Variables reviewed included age distribution, sex, frequency of AECB events over the prior year, AECB-related admissions, previous illnesses, allergy reports, and relevant family background. No measurable differences appeared across the groups ($p > 0.05$), indicating that random assignment produced equivalent baseline conditions.

Table 1. Baseline Demographic Features of the Three Cohorts

Characteristics	Experimental Group (n=119)	Positive Drug Control Group (n=120)	Blank Control Group (n=60)
Age (years)	55.91 ± 13.02 (25–75)	56.24 ± 12.96 (20–75)	51.78 ± 15.01 (21–73)
Gender (Male/Female)	47.90% / 52.10%	58.33% / 41.67%	43.33% / 56.67%
Number of acute exacerbations of chronic bronchitis (AECB) in the past year	0.95 ± 1.02 (0–3)	0.91 ± 1.04 (0–4)	1.00 ± 1.21 (0–4)
Number of hospitalizations due to AECB in the past year	0.26 ± 0.50 (0–2)	0.26 ± 0.50 (0–2)	0.28 ± 0.59 (0–2)
Past medical history (with concomitant diseases)	23.53%	27.50%	20.00%
History of allergy	1.68%	1.67%	1.67%
Family history (of related diseases)	0.00%	0.83%	0.00%

Compliance and concomitant medication

Participants in the experimental arm used a total of 496.55 ± 21.41 bags, with treatment lasting an average of 24.18 ± 0.90 weeks; adherence within the 80%–120% range reached 100%. In the active drug control arm, the cumulative amount taken was 1475.78 ± 150.38 capsules, and the mean duration of dosing was 23.92 ± 2.21 weeks, yielding a compliance level of 99.17%.

During the treatment period, concomitant medication was used in 47 individuals (92 episodes; 39.50%) in the experimental arm, 61 individuals (109 episodes; 50.83%) in the active drug control group, and 37 individuals (88 episodes; 61.67%) in the blank control arm. In the follow-up phase, the numbers were 26 individuals (48 episodes; 21.85%) in the experimental group, 55 individuals (101 episodes; 45.83%) in the drug control group, and 27 individuals (58 episodes; 45.00%) in the blank control group.

Efficacy outcomes

According to **Figure 2**, both treatment groups exhibited substantial decreases in CB symptom measurements after 24 weeks ($p < 0.05$ relative to baseline). Statistical comparisons showed clear distinctions among the three groups throughout therapy (all $p < 0.001$), and direct contrasts between the two treatment groups were also significant (all $p < 0.05$). At the 24-week follow-up, significant within-group and between-group differences in CB symptom scores remained (all $p < 0.05$).

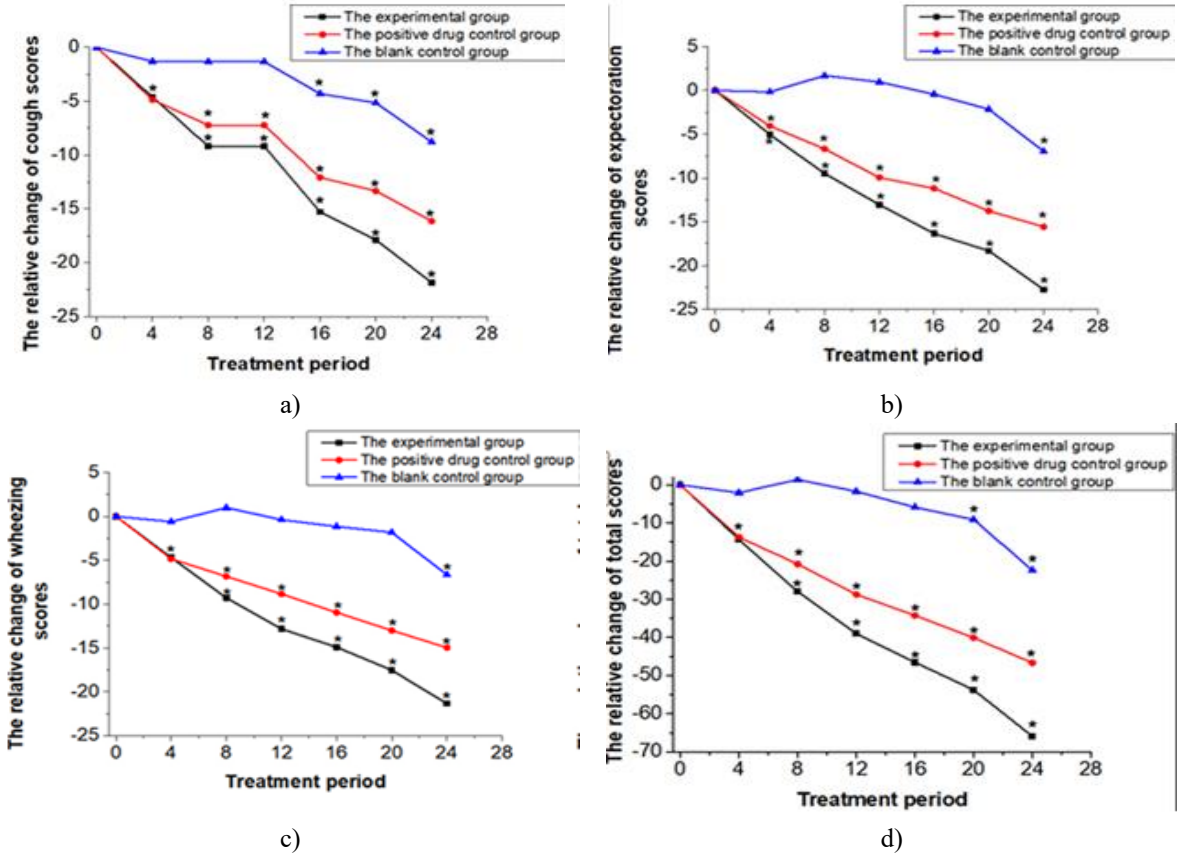

Figure 2. Shows how cough, sputum output, and wheezing shifted over time in the experimental, positive drug control, and blank control arms. *p < 0.05.

When examining AECB outcomes after treatment, the mean duration before the first recorded AECB episode was 131.41 ± 101.71 days in the experimental arm, 130.29 ± 96.34 days in the positive drug group, and 84.73 ± 63.05 days in the blank control arm (p = 0.0219). The longest spacing between consecutive AECB events appeared in the experimental cohort at 157.75 ± 69.86 days, compared with 119.91 ± 63.48 days in the positive drug control arm and 110.43 ± 53.13 days in the blank control arm (p = 0.3401). AECB episodes were briefest in the experimental group (6.59 ± 4.68 days), whereas the positive drug and blank controls experienced episodes lasting 8.18 ± 5.49 days and 12.81 ± 8.08 days, respectively (p = 0.0002). Average AECB severity scores were 1.25, 1.33, and 1.50 for the experimental, positive drug, and blank control groups (p = 0.0218). The number of AECB attacks per person was lowest in the experimental arm at 0.33 ± 0.54, compared with 0.84 ± 0.93 in the drug control group and 1.34 ± 1.32 in the blank control group (p < 0.0001). Except for the interval between episodes, every other AECB-related indicator differed significantly between the treatment arms and the blank control (all p < 0.05). Both FAS and PPS evaluations likewise confirmed significant contrasts in AECB duration and episode frequency (p < 0.05; **(Table 2)**).

Table 2. AECB Outcomes in the Three Groups Following Treatment

Items	Experimental Group	Positive Drug Control Group	Blank Control Group	P-value between groups (FAS)	P-value between groups (PPS)
Time to first AECB occurrence (days)	131.41 ± 101.71	130.29 ± 96.34	84.73 ± 63.05	0.0333	>0.05
Interval between AECB occurrences (days)	157.75 ± 69.86	119.91 ± 63.48	110.43 ± 53.13	0.3401	>0.05
Duration of AECB episodes (days)	6.59 ± 4.68	8.18 ± 5.49	12.81 ± 8.08	<0.001	<0.001
Severity of AECB (score)	1.25 (Q1=1.00, Q3=1.50)	1.33 (Q1=1.00, Q3=1.67)	1.50 (Q1=1.22, Q3=1.67)	0.0356	>0.05
Frequency of AECB occurrences (times/year)	0.33 ± 0.54	0.84 ± 0.93	1.34 ± 1.32	<0.001	<0.001

With respect to lung function, no measurable alterations were found after 24 weeks in FEV1/FVC%, FEV1%pred, PEF, MMEF, FVC, or FEV1 for any study arm (all $p > 0.05$; **(Table 3)**). Thus, none of the groups showed functional respiratory improvement over the course of the study.

Table 3. Pulmonary and Immune Measurements After 24 Weeks

Items	Experimental Group		Positive Drug Control Group		Blank Control Group	
	Baseline	Change at 24 Weeks	Baseline	Change at 24 Weeks	Baseline	Change at 24 Weeks
Pulmonary Function Indicators						
FEV1/FVC (%)	72.78 ± 17.51	1.99 ± 11.08	70.56 ± 17.98	2.80 ± 9.81	77.18 ± 13.07	0.23 ± 9.83
FEV1 % predicted	80.47 ± 27.58	0.13 ± 18.72	78.59 ± 24.49	1.99 ± 17.08	86.48 ± 22.21	−0.38 ± 19.27
PEF (mL/min)	5121.03 ± 2225.68	440.78 ± 1727.97	5250.08 ± 2260.68	258.47 ± 1785.03	6186.08 ± 2376.29	−142.75 ± 2140.24
MMEF (mL/min)	2108.66 ± 1298.94	128.48 ± 1090.19	2149.71 ± 1452.44	−10.94 ± 874.11	2509.61 ± 1359.49	−1.05 ± 1208.37
FVC (mL)	2861.47 ± 911.99	65.50 ± 670.75	3044.48 ± 890.45	−77.03 ± 639.40	3105.31 ± 892.60	−24.04 ± 717.72
FEV1 (mL)	2164.89 ± 883.54	78.36 ± 633.09	2211.53 ± 895.83	17.10 ± 581.82	2429.36 ± 817.62	−25.07 ± 597.94
Immune Indicators						
$CD4^+$ (cells/μL)	767.25 ± 239.43	175.50 ± 429.66	1091.50 ± 369.23	−124.00 ± 103.94	629.50 ± 287.79	212.00 ± x1
$CD8^+$ (cells/μL)	649.25 ± 478.75	31.50 ± 261.29	840.50 ± 353.79	−112.67 ± 211.53	475.00 ± 46.67	69.00 ± x2
$CD4^+/CD8^+$ ratio	1.61 ± 1.15	−0.07 ± 0.52	1.36 ± 0.30	−0.05 ± 0.30	1.31 ± 0.47	0.17 ± x3

Notes: X1, X2, and X3 indicate missing entries, which resulted from limited immunologic testing capacity at multiple participating sites.

In terms of immune indicators **(Table 3)**, no meaningful variation was detected among the three study arms for CD4+ ($p = 0.5105$), CD8+ ($p = 0.7045$), or the CD4+/CD8+ ratio ($p = 0.8882$).

For the quality-of-life assessment, notable gains were recorded in mobility, personal care, routine tasks, and overall health perception in all groups following 24 weeks of therapy (all $p < 0.05$). Conversely, pain/discomfort and anxiety/depression showed no measurable change.

Adverse events

According to **Table 4**, the experimental arm experienced 14 individuals with adverse events during treatment (15 total episodes), corresponding to an incidence of 11.75%. Most events fell under infectious or invasive conditions—12 individuals (12 episodes), with a rate of 10.08%—potentially linked to the brief period of drug exposure. No adverse events were noted for this group during the follow-up phase. Reported issues included upper respiratory infections, pharyngitis, and acute bronchitis.

Table 4. Adverse Events During Treatment and Follow-up

Adverse Event Category	Group	n	Overall Adverse Events	Drug-Related Adverse Events	Severe Adverse Events	Seriously Drug-Related Adverse Events	Adverse Events Leading to Withdrawal	Drug-Related Adverse Events Leading to Withdrawal
			Times / Cases / Incidence (%)	Times / Cases / Incidence (%)	Times / Cases / Incidence (%)	Times / Cases / Incidence (%)	Times / Cases / Incidence (%)	Times / Cases / Incidence (%)
Treatment Period								
	Experimental Group	119	15 / 14 / 11.76%	0 / 0 / 0.00%	2 / 2 / 1.68%	0 / 0 / 0.00%	2 / 2 / 1.68%	0 / 0 / 0.00%

Positive Drug Control Group	120	8 / 8 / 6.67%	1 / 1 / 0.83%	0 / 0 / 0.00%	0 / 0 / 0.00%	1 / 1 / 0.83%	1 / 1 / 0.83%
Blank Control Group	59	2 / 2 / 3.39%	0 / 0 / 0.00%	0 / 0 / 0.00%	0 / 0 / 0.00%	0 / 0 / 0.00%	0 / 0 / 0.00%
Total	298	25 / 24 / 8.05%	1 / 1 / 0.34%	2 / 2 / 0.67%	0 / 0 / 0.00%	3 / 3 / 1.01%	1 / 1 / 0.34%
Follow-up Period							
Experimental Group	119	0 / 0 / 0.00%	0 / 0 / 0.00%	0 / 0 / 0.00%	0 / 0 / 0.00%	0 / 0 / 0.00%	0 / 0 / 0.00%
Positive Drug Control Group	120	4 / 1 / 0.83%	0 / 0 / 0.00%	0 / 0 / 0.00%	0 / 0 / 0.00%	0 / 0 / 0.00%	0 / 0 / 0.00%
Blank Control Group	59	0 / 0 / 0.00%	0 / 0 / 0.00%	0 / 0 / 0.00%	0 / 0 / 0.00%	0 / 0 / 0.00%	0 / 0 / 0.00%
Total	298	4 / 1 / 0.34%	0 / 0 / 0.00%	0 / 0 / 0.00%	0 / 0 / 0.00%	0 / 0 / 0.00%	0 / 0 / 0.00%

The rising prevalence of chronic bronchitis has been strongly tied to factors such as worsening air quality, cigarette exposure, and demographic aging [3-6]. Within clinical settings, Chinese proprietary medicines retain appeal due to ease of use, tolerability, and distinctive therapeutic patterns [24].

Traditional theory classifies CB under several pathological categories—"cough," "asthma-type disorders," and "phlegm stasis"—usually involving functional disturbance of the lung, spleen, and kidney systems. Early classical writings, such as Zhang Zhongjing's Synopsis of the Golden Chamber [25], identified "warming the lung and transforming phlegm" as a guiding strategy, inspiring herbal formulations including Xiaoqinglong Decoction, Linggan Wuwei Jiangxin Decoction, and Shegan Mahuang Decoction [25].

Contemporary pharmacological inquiries suggest that Xiaoqinglong Decoction may regulate the PI3K–AKT signaling axis [26], whereas Linggan Wuwei Jiangxin Decoction appears to lower IL-2 and IL-4 while elevating aquaporin-1, thereby influencing airway inflammation and secretion dynamics [27].

This randomized multi-center investigation compared Guben Kechuan Granules (n=119) with a standard comparator, Guilong Kechuanning Capsules (n=120), and with a blank group (n=60).

Participants taking the investigational granules experienced marked reductions in all CB-related symptoms—cough, sputum, and wheeze—during the 24-week treatment period and maintained these improvements through the subsequent 24-week observation window, outperforming both comparison groups (all $p<0.05$).

Because acute exacerbations represent sudden deterioration of CB, the findings indicate that the granules delayed the onset of the first AECB, shortened the length of each episode, reduced episode intensity, and lowered event frequency, relative to the blank control (all $p<0.05$).

Quality-of-life domains—ambulation, self-maintenance, daily function, and general health perception—also improved noticeably after 24 weeks of therapy.

Despite these multiline clinical gains, spirometry did not show measurable improvement, possibly due to the relatively mild initial impairment and the limited intervention duration.

These results indicate that Guben Kechuan Granules may serve as a valuable therapeutic option for managing CB. Comparable outcomes have been noted in research on Bailing capsules, where individuals showed marked relief in CB manifestations and fewer AECB incidents after 48 weeks of therapy and follow-up [18]. Additionally, treatment with OM-85 for 12 weeks has been reported to decrease the occurrence of acute flare-ups in CB and demonstrates good tolerability [28]. Another investigation documented that a combined regimen of Hedera helix (ivy) leaf extract with Coptidis Rhizome Syrup helped ease bronchitic complaints and enhanced respiratory-related quality of life among CB patients [29].

Crucially, participants in the experimental arm reported no adverse events throughout the observation period. Regarding lung function, indices such as PEF, MMFE, FVC, and FEV1 increased more noticeably in the experimental cohort than in the control groups following 24 weeks of intervention; nonetheless, these gains did not reach statistical significance. This may stem not only from the limited baseline severity but also from the predominance of mild cases rather than sample size constraints alone. Future investigations would benefit from enrolling a larger population and prolonging treatment to clarify the effects of Guben Kechuan Granules on respiratory function. Although the clinical benefits appear encouraging, the exact biological pathways responsible for these effects remain to be precisely defined. Gu-Ben-Ke-Chuan decoction—listed in the Chinese Pharmacopeia and licensed by the China Food and Drug Administration [30]—has previously been associated with modulation of TNF-related anti-inflammatory signaling based on integrated systems pharmacology and surface plasmon resonance analyses [31]. Other evidence suggests that Guben Kechuan Granules may influence

immune regulation by adjusting T-cell subset distribution and altering thymus and spleen indices in COPD models [32].

Several limitations should be acknowledged. Concurrent medication use could have shaped the clinical response to Guben Kechuan Granules, introducing heterogeneity into the data. Additionally, the relatively modest sample size may have reduced the ability to detect significant differences, especially in pulmonary function metrics. Furthermore, the study did not incorporate standardized mechanistic experiments to identify the pathways responsible for the observed therapeutic outcomes.

Given that inflammatory mediators play a central role in CB pathophysiology [33], upcoming research should explore whether Guben Kechuan Granules modulate molecules such as IL-1, IL-6, and TNF-α. Clarifying these interactions would provide more robust scientific support for their clinical application. Although antibiotic and supportive treatments for AECB were restricted by protocol, their use may still have contributed to symptom improvement, representing a potential confounder.

Conclusion

The findings indicate that Guben Kechuan Granules can ease CB symptoms, diminish the intensity of AECB, and reduce the frequency of AECB events, thereby representing a potentially valuable option for affected individuals. Mechanistic analyses are currently ongoing at the Artemisinin Research Center of the Chinese Academy of Traditional Chinese Medicine. Broad, multi-nation recruitment will be required for large, multi-center trials capable of generating high-quality evidence to support worldwide clinical use. While notable improvement in symptoms and AECB reduction was observed, lung-function parameters showed no statistically significant change throughout the 24-week treatment duration.

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