



# Comparative Effectiveness of Carbazochrome Sulphonate (AC-17) Combined with Vitamin C and Vitamin K Versus Vitamin C and Vitamin K in Managing Hemoptysis in Pulmonary Tuberculosis Patients

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## KEYWORDS

Pulmonary tuberculosis, hemoptysis, carbazochrome sulfonate, vitamin K, vitamin C, hemostasis

## ABSTRACT:

**Background and Objectives.** Hemoptysis is a common and severe complication of pulmonary tuberculosis (TB), often requiring prompt intervention. While conventional therapies with vitamin K and C are used, their effectiveness may be limited in cases of significant vascular damage. Carbazochrome Sulfonate (AC-17) has been suggested as a potential adjunctive treatment to enhance hemostasis. This study aimed to evaluate the efficacy of Carbazochrome Sulfonate (AC-17) in combination with vitamin K and vitamin C, compared to vitamin K and C alone, in reducing the duration of hemoptysis in patients with pulmonary TB.

**Materials and Methods.** A comparative observational study was conducted at Wahidin Sudirohusodo Hospital and Labuang Baji Hospital, involving 60 pulmonary TB patients with hemoptysis. The treatment group received AC-17 (50 mg IV) along with vitamin K and C, while the control group received only vitamins K and C. The primary outcome was the duration of hemoptysis, and statistical analysis was performed using Chi-square and t-tests.

**Results.** The treatment group had a significantly shorter mean duration of hemoptysis (4.03 days) compared to the control group (6.56 days;  $p = 0.002$ ). Ninety-three percent of the treatment group stopped bleeding within 7 days, compared to 50% in the control group.

**Conclusions.** AC-17, when combined with vitamin K and C, significantly reduced the duration of hemoptysis in pulmonary TB patients. These findings suggest AC-17 as an effective adjunct in hemostatic therapy for TB-related hemoptysis.

## 1. Introduction

Hemoptysis refers to the coughing up of blood from the lower respiratory tract, which may present as blood-tinged sputum or pure blood without mucus.<sup>1</sup> It is a frequent clinical complication in patients with pulmonary tuberculosis (TB), with a reported prevalence approximately 8% depending on the extent of parenchymal destruction and pulmonary vascular

involvement.<sup>2</sup> Tuberculosis remains the leading etiology of hemoptysis in high-burden countries, accounting for the majority of moderate to severe cases. Bleeding in TB occurs due to chronic inflammation, tissue necrosis, and erosion of bronchial or pulmonary vessels, which may progress to massive hemoptysis and substantially increase mortality risk.<sup>3</sup> Therefore, rapid and effective hemorrhage control is a critical component of pulmonary TB management.



Conventional therapeutic approaches to control hemoptysis in pulmonary TB include administration of vitamin K and vitamin C. Vitamin K plays an essential role in hepatic synthesis of clotting factors II, VII, IX, and X, thereby supporting the coagulation cascade.<sup>4,5</sup> Meanwhile, vitamin C contributes to the maintenance of vascular integrity by promoting collagen synthesis and preventing capillary fragility.<sup>6</sup> However, in many cases, these measures alone may not be sufficient to achieve rapid hemostasis, particularly when bleeding is due to vascular damage or increased capillary permeability.

Carbazochrome sulfonate sodium (AC-17) is a hemostatic agent that acts by reducing capillary permeability, enhancing endothelial stability, and improving platelet function.<sup>7</sup> Several studies have suggested that AC-17 can shorten bleeding time and improve clinical outcomes when used in combination with conventional hemostatic therapy.<sup>8</sup> Nevertheless, evidence regarding its effectiveness in hemoptysis caused by pulmonary tuberculosis remains limited.

Therefore, this study aimed to evaluate the effectiveness of Carbazochrome Sulfonate (AC-17) combined with vitamin K and vitamin C compared to vitamin K and vitamin C alone in stopping hemoptysis among patients with pulmonary tuberculosis infection. The findings of this study are expected to provide additional insight into the optimization of hemostatic therapy in TB-related hemoptysis.

## 2. Methods

### *Study Design*

This study employed a comparative observational design involving two groups of newly diagnosed pulmonary tuberculosis patients presenting with hemoptysis. The treatment group received Carbazochrome sulfonate (AC-17) in combination with Vitamin C and Vitamin K, while the control group received Vitamin C and Vitamin K alone. The sampling technique used is purposive sampling, and the study will be conducted at Labuang Baji Hospital and Dr. Wahidin Sudirohusodo Hospital from August to October 2025. Data collection involved reviewing medical records.

Participants were not randomized, and treatment assignment was based on clinical judgment and patient availability of the drug. The primary outcome was the

duration of hemoptysis (in days), and comparisons between groups were analyzed using the Chi-square test.

### *Study Setting and Period*

The study was conducted at Dr. Wahidin Sudirohusodo Hospital and Labuang Baji Hospital, Makassar, Indonesia. Data collection began after receiving institutional approval and continued until the required sample size was achieved between August and October 2025. Data collection involved reviewing medical records.

### *Study Population*

The target population in this study consisted of all patients coughing up blood caused by pulmonary tuberculosis. The accessible population included patients who sought treatment at Dr. Wahidin Sudirohusodo Hospital and Labuan Baji Hospital, experienced coughing up blood, and were diagnosed with pulmonary tuberculosis based on supporting examinations during the study period.

### *Eligibility Criteria*

Eligibility criteria were applied to ensure the inclusion of appropriate study participants. Individuals were eligible for enrollment if they were 18 years of age or older, presenting with hemoptysis due to pulmonary tuberculosis, whether they are newly diagnosed or undergoing ongoing treatment. All participants must have a confirmed diagnosis of pulmonary tuberculosis, either through microbiological testing or radiological imaging. Additionally, only patients who provide written informed consent to participate in the study will be included.

### *Data Collection*

The study sample consists of all patients with pulmonary tuberculosis who present with either massive or non-massive hemoptysis at Labuang Baji Hospital and Dr. Wahidin Sudirohusodo Hospital (including both new cases of pulmonary tuberculosis or those undergoing ongoing treatment). The sample will receive interventions starting from the time of admission to the emergency department (ED) until hemoptysis ceases during hospitalization, which will be either within a maximum of 7 days or after 24 hours of being free from hemoptysis. The intervention consists of Carbazochrome 50 mg intravenous three times a day, in addition to



Vitamin K 10 mg and Vitamin C 200 mg intravenous three times a day. The control group will receive only Vitamin K 10 mg and Vitamin C 200 mg intravenous three times a day.

### **Statistical Analysis**

All statistical analyses were performed using SPSS version 20.0 (Armonk, NY, USA; IBM Corp.). Descriptive statistics were utilized to summarize the baseline characteristics of the study participants. Categorical variables were analyzed using the Chi-square test and Fisher's exact test. For numerical data, comparisons were performed using paired *t*-tests. *P* < 0.05 was considered statistically significant.

### **Ethical Approval**

This research was approved by the Health Research Ethics Committee of the Faculty of Medicine, Hasanuddin University-Wahidin Sudirohusodo Hospital Makassar (ethical number 771/UN4.6.4.5.31/PP36/2024) on September 26, 2024. Written informed consent was obtained from all participants.

## **3. Results**

### **Patient Characteristics**

A total of 60 newly diagnosed pulmonary tuberculosis (TB) patients with hemoptysis were included in this study, consisting of 30 patients in the treatment group (Carbazochrome sulfonate [AC-17] + Vitamin C + Vitamin K) and 30 in the control group (Vitamin C + Vitamin K only). The baseline characteristics of both groups were comparable (Table 1).

The mean age of patients in the treatment group was 44.3 years (range 22–72 years), and in the control group 45.9 years (range 20–88 years). Most patients were aged 40–60 years in both groups (66.7% in treatment vs. 40% in control). Females were slightly more common (56.7%) in the treatment group. The majority of patients presented with non-massive hemoptysis (66.7% in treatment vs. 70% in control).

Radiological findings showed minimal lesions in most patients (66.7% in treatment vs. 70% in control). Based on bacteriological assessment using GeneXpert MTB/RIF (RMT), low bacillary load predominated in both groups (53.3% in treatment vs. 56.7% in control).

### **Effect of Treatment on Duration of Hemoptysis**

A significant difference was observed between the treatment and control groups regarding the duration of hemoptysis (*p* = 0.002). In the treatment group, 93.3% of patients experienced cessation of hemoptysis within <7 days, with a mean duration of 4.03 days (median: 4 days; range: 2–7 days). Conversely, in the control group, only 50% recovered within <7 days, with a mean duration of 6.56 days (median: 6.5 days; range: 3–14 days) (Table 2). These findings indicate that administration of Carbazochrome sulfonate (AC-17) supplemented with Vitamin C and Vitamin K significantly shortened the duration of bleeding compared to Vitamin C and K alone.

### **Association Between Radiologic Lesion Extent and Duration of Hemoptysis**

Within the treatment group, patients with minimal radiologic lesions tended to have faster resolution of hemoptysis compared to those with extensive lesions (20 patients <7 days vs. 8 patients ≥7 days), though the association did not reach statistical significance (*p* = 0.103).

### **Association Between Bacteriological Burden and Duration of Hemoptysis**

No significant correlation was found between RMT (GeneXpert) bacterial load and duration of hemoptysis in the treatment group (*p* = 0.19). However, patients with lower bacillary loads showed a trend toward faster resolution of bleeding.

## **4. Discussion**

The present study demonstrates that the addition of Carbazochrome Sulfonate (AC-17) to standard hemostatic therapy consisting of vitamin K and vitamin C significantly accelerates the cessation of hemoptysis among patients with pulmonary tuberculosis. The mean duration of bleeding was markedly shorter in the AC-17-supplemented group (4.03 days) than in the control group receiving only vitamins K and C (6.56 days, *p* = 0.002). These findings suggest that AC-17 exerts an additive hemostatic effect that is clinically meaningful in pulmonary tuberculosis-related hemorrhage.



## ***Pathophysiology of Hemoptysis in Pulmonary Tuberculosis***

Hemoptysis in pulmonary TB results from destruction of bronchial and pulmonary vessels due to chronic granulomatous inflammation, cavitary necrosis, and rupture of hypertrophied bronchial arteries.<sup>2,9,10</sup> Recurrent inflammation induces vascular remodeling, pseudoaneurysm formation (Rasmussen's aneurysm), and friable neovascularization that predispose to bleeding.<sup>3</sup> The high mortality associated with massive hemoptysis underscores the need for rapid hemorrhage control.<sup>11,12</sup>

## ***Mechanistic Basis of the Therapeutic Combination***

Vitamin K is essential for hepatic synthesis of  $\gamma$ -carboxylated coagulation factors II, VII, IX, and X, thus supporting secondary hemostasis.<sup>4,13</sup> Vitamin C, in contrast, acts primarily on vascular integrity by promoting collagen hydroxylation and endothelial repair.<sup>6</sup> Nevertheless, these vitamins alone may not counteract microvascular fragility and capillary leakage caused by chronic infection and inflammation.

Carbazochrome Sulfonate Sodium (AC-17) enhances primary hemostasis through capillary stabilization, decreased permeability, and modulation of platelet function.<sup>7</sup> Experimental data indicate that AC-17 inhibits phosphatidylinositol hydrolysis and restores endothelial barrier function, thereby reducing extravasation.<sup>7</sup> Clinical studies in surgical and trauma settings have shown that AC-17, particularly when combined with antifibrinolytic agents or vitamins, reduces blood loss and inflammatory responses.<sup>8,14-16</sup>

## ***Comparison With Previous Studies***

Although research on AC-17 in TB-related hemoptysis is scarce, similar effects have been reported in other hemorrhagic conditions. In obstetric, orthopedic, and neurosurgical populations, AC-17 administration shortened bleeding time and reduced transfusion requirements.<sup>8,16-18</sup> In clinical and surgical settings, carbazochrome sodium sulfonate has been reported to enhance vascular stability and support platelet-related hemostasis, leading to reduced bleeding and transfusion needs, especially when combined with tranexamic acid during orthopedic or trauma surgery.<sup>14,16-18</sup> Moreover, combined use of AC-17 with vitamin K accelerated recovery in patients with chronic subdural hematoma.<sup>19</sup>

Although randomized data are limited, several clinical reports and series have described that medical therapy including carbazochrome sodium sulfonate (often combined with tranexamic acid or other supportive agents) may contribute to hematoma resorption and clinical recovery in patients with chronic subdural hematoma.<sup>19-21</sup> These findings align with the current study's observation that AC-17 provides additional benefit beyond conventional vitamin therapy.

## ***Influence of Radiologic Lesions and Bacillary Load***

Although our study did not find a statistically significant correlation between the extent of radiologic lesions and duration of hemoptysis, patients with minimal lesions showed a trend toward faster cessation. This may reflect less severe parenchymal destruction and lower vascular involvement.<sup>22-24</sup> Similarly, a lower GeneXpert (RMT) bacillary load was associated with more rapid resolution of bleeding, consistent with reports that high bacterial burden correlates with persistent inflammation and tissue necrosis.<sup>25-27</sup>

## ***Potential Mechanisms of AC-17 Efficacy***

The observed improvement in hemostasis can be attributed to several mechanisms. First, AC-17 strengthens endothelial tight junctions and limits inflammatory mediator-induced permeability.<sup>7</sup> Second, it may enhance platelet adhesion and aggregation at damaged vascular sites.<sup>28</sup> Third, by reducing local oxidative stress and microvascular inflammation, AC-17 can synergize with vitamin C to restore vascular homeostasis.<sup>28-31</sup> These complementary actions explain the shorter duration of bleeding seen in our treatment group.

## ***Clinical Implications***

Given that hemoptysis remains a major cause of emergency admissions among tuberculosis patients in high-burden regions,<sup>32-35</sup> the use of AC-17 as an adjunctive hemostatic agent may improve patient outcomes and reduce hospitalization duration. The regimen is relatively safe, inexpensive, and well tolerated when administered intravenously at the studied doses.<sup>8,16,18,28</sup> Furthermore, integrating AC-17 into standard tuberculosis management protocols could be particularly beneficial in resource-limited settings where interventional radiology or surgical embolization is unavailable.<sup>28</sup>



## 5. Limitations

This study is limited by its non-randomized design and modest sample size, which may introduce selection bias. Treatment allocation based on drug availability and clinician judgment could confound outcomes. To better assess the overall impact on pulmonary tuberculosis (TB) infection, it would be more comprehensive to include all cases of pulmonary TB, rather than focusing solely on newly diagnosed cases. Additionally, laboratory coagulation parameters and inflammatory markers (e.g., fibrinogen, D-dimer, CRP) were not systematically assessed. Future randomized controlled trials should incorporate these parameters to confirm causality and further elucidate the mechanisms by which AC-17 modulates hemostasis in pulmonary tuberculosis.

## 6. Conclusion

In summary, therapy with vitamin K and vitamin C combination with Carbazochrome Sulfonate (AC-17) significantly reduced the duration of hemoptysis in patients with pulmonary tuberculosis compared with vitamin therapy alone. The findings support the adjunctive use of AC-17 to enhance vascular stability and expedite hemostasis in tuberculosis-related bleeding. Further multicenter randomized studies are warranted to validate these results and optimize dosage strategies.

## 7. Declarations

### Conflict of Interest

The authors affirm that there are no conflicts of interest to declare in relation to the publication of this research

### Author's Contributions

JM was responsible for the coordination, research, data collection, analysis and interpretation, as well as report writing. RAN supported data collection and assisted with data analysis. Also SN, BN contributed to the research design and data collection.

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## TABLES

Table 1. Patient baseline characteristics of new cases of pulmonary tuberculosis patients

Variable		Case		Control	
		n	%	n	%
<b>Age (years)</b>	Min-Max	22-72		20-88	
	18-<40	8	26,7	16	53,3
	40-60	20	66,7	12	40
	>=60	2	6,7	2	6,7
<b>Gender</b>	Male	13	43,3	14	46,7
	Female	17	56,7	16	53,3
<b>Characteristic of Hemoptysis</b>	Masiv	10	33,3	9	30
	Non Massive	20	66,7	21	70
<b>Length of Hemoptysis</b>	Min-Max	2-7 days		3-14 days	
	<7 days	28	93,3	15	50
	>=7 days	2	6,7	15	50
	Median	4 days		6,5 days	
	Mean	4,03 days		6,56 days	
<b>Radiology</b>	Extensive lesion	10	33,3	9	30
	Minimal Lesion	20	66,7	21	70
<b>RMT</b>	High	8	26,7	6	20
	Medium	6	20	7	23,3
	Low	16	53,3	17	56,7

Table 2. The relationship between the treatment group and the control group on the duration of hemoptysis



Variable	Length Hemoptysis		p-value
	<7 days	≥ 7 days	
Case	28	2	0,002
Control	15	15	

\*Chi-squares test

Table 3. The relationship between radiological lesion area and hemoptysis duration of pulmonary TB patients receiving treatment

Variable	Length of Hemoptysis		p-value
	<7 days	≥ 7 days	
<b>X-ray of lesion</b>			
Wide Lesion	8	2	0,103
Minimal Lesion	20	0	

\*Chi square test, McNemar test

Table 4. Correlation between RMT bacteriological examination and duration of hemoptysis in treatment group

Variable	Length of Hemoptysis		p-value
	<7 days	≥ 7 days	
<b>RMT</b>			
High	7	1	0,19
Medium	6	0	
Low	16	1	