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Study on the chain effect of key pharmaceutical attributes of emergency trauma hemostatic drugs on physician preferences, clinical efficacy and pharmacoeconomic outcomes

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Abstract: This study constructed a chain analysis model linking pharmaceutical attributes, physician preferences, clinical efficacy and pharmacoeconomic outcomes. Using multicenter prospective data, we analyzed the multi-level mechanisms influencing the key pharmaceutical attributes of emergency trauma hemostatics. A total of 1,500 patients from six hospitals in China were included. The pharmacological properties of tranexamic acid, ethamide and hemocoagulase were analyzed and their impact on physician preferences, efficacy and economic outcomes was assessed. Results showed that antifibrinolytic mechanism (weighted 38.2%), onset of action (29.7%) and thrombotic risk (24.1%) were the core attributes influencing physician preferences. Due to its advantageous pharmaceutical attributes, tranexamic acid had the shortest hemostatic time (14.5 ± 3.0 minutes), the lowest 24-hour blood transfusion volume (320 ± 70 ml) and the best cost-effectiveness (328.6 yuan/minute). This study provides evidence-based guidance for the precise selection of hemostatics based on pharmaceutical attributes.

Keywords: Emergency trauma; Hemostatics; Pharmaceutical attributes; Pharmacoeconomics; Physician preferences

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INTRODUCTION

In the treatment of traumatic bleeding in emergency department, the clinical application of hemostatic drugs is highly heterogeneous and there are significant differences in drug selection among different levels of hospitals and doctors of different years of experience. The essence of this difference is the matching process between the pharmaceutical properties of drugs and the needs of clinical decision-making. The intrinsic characteristics of hemostatic drugs, such as the mechanism of action, speed of onset and safety, shape doctors' cognition and form preferences, ultimately affecting treatment outcomes and health resource allocation (Yanwei *et al*., 2025).

Globally, traumatic bleeding is the leading cause of early death in trauma patients. Statistics from the World Health Organization show that more than 1.9 million people die each year from traumatic bleeding, of which about 30% die from failure to stop bleeding in a timely and effective manner (Chester *et al*., 2024). Within the "golden hour" of emergency treatment, the rational choice of hemostatic drugs is directly related to the patient's survival prognosis. However, in clinical practice, there are huge differences in drug use among hospitals of different levels (Lei *et al*., 2023). Data show that the use rate of tranexamic acid in tertiary hospitals reaches 62%, while that in secondary hospitals is only 28% (Shaojun *et al*., 2024). This difference is not only a reflection of the uneven distribution of medical resources, but also reflects the cognitive gap between medical workers in the logic of matching the pharmaceutical properties of hemostatic drugs with clinical needs.

Existing studies mostly focus on the superficial correlation between drug use behavior and efficacy and lack in-depth analysis of pharmaceutical properties as the source of decision-making. For example, the difference in efficacy between tranexamic acid and sulfonamide is actually due to the different biological characteristics of the antifibrinolytic mechanism and platelet enhancement mechanism (El Baser *et al*., 2021); the drug use tendency of different medical institutions is also related to the priority judgment of attributes such as drug administration convenience and dosage form stability. Most studies only compare the efficacy of a single drug, such as tranexamic acid and placebo, but ignore the intrinsic connection between different drug mechanisms of action, such as antifibrinolysis and platelet enhancement and trauma pathophysiology, such as the degree of hyperfibrinolysis (Muhammad *et al*., 2024). At the same time, in terms of pharmacoeconomic analysis, most of them are limited to the comparison of drug unit prices and do not take into account the chain transmission of "attribute-efficacy-cost", such as the impact of shortened onset time on blood transfusion costs (Mastrorilli *et al*., 2022).

The objective of this study is to take the key pharmaceutical attributes of emergency trauma hemostatic drugs as the core starting point, construct a chain analysis framework linking pharmaceutical attributes, physician preferences, clinical efficacy and pharmacoeconomic

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outcomes and quantitatively analyze the multi-level influence mechanism of key pharmaceutical attributes on the above three dimensions. By clarifying the intrinsic logic of how pharmaceutical attributes shape clinical decision-making and treatment outcomes, this study aims to fill the gap in existing research that lacks in-depth exploration of pharmaceutical attributes as decision sources and further provide evidence-based support for the precise selection of hemostatic drugs in clinical practice, as well as a reference basis for the formulation of clinical pharmacy management strategies and drug-related health policies.

MATERIALS AND METHODS

Study design

This multicenter, prospective, observational study was conducted from January 2021 to January 2025 in the emergency departments of three Class A tertiary hospitals and three Class A secondary hospitals in the eastern, central and western regions of China with varying economic levels.

Study participants

Patients aged 18-65 years with active bleeding from trauma who had hemostatic therapy initiated within 30 minutes were included. Patients with hematologic disorders, those undergoing anticoagulant/thrombolytic therapy, those who were pregnant or lactating, or those with severe liver or renal impairment were excluded. A total of 1,500 cases were included, including 975 males (65%) and 525 females (35%), with an average age of (39.2±10.8) years. The causes of trauma included traffic accidents in 675 cases (45%), falls from height in 420 cases (28%), sharp injuries in 255 cases (17%) and violent assaults in 150 cases (10%). The baseline between-group balance was good (p>0.05).

Definition and quantification of key pharmaceutical attributes

Six core attributes were determined by the Delphi method among 15 emergency pharmacy and trauma medicine experts and quantified using a 3-point scale (the higher the score, the better the attribute) (Timothy *et al*., 2025):

Mechanism of action: antifibrinolysis (tranexamic acid) = 3 points, platelet enhancement (ethylamine) = 2 points, thrombin-like effect (thrombin) = 1 point. *Onset of action*: <5 minutes = 3 points, 5-10 minutes = 2 points, >10 minutes = 1 point.
Half-life: >6 hours = 3 points, 2-6 hours = 2 points, <2 hours = 1 point.
Thrombotic risk: Low (tranexamic acid) = 3 points, Moderate (etamipine) = 2 points, High (hemocoagulase) = 1 point.
Ease of administration: IV push = 3 points, IV drip = 2 points, Intramuscular injection = 1 point.
Dosage form stability: Room temperature storage = 3 points, refrigeration required = 2 points, ready for immediate use = 1 point.

Observation indicators

Efficacy in-depth indicators

Initial bleeding volume classification: According to the cumulative bleeding volume within 30 minutes after trauma, it is divided into Class A (<500ml), Class B (500-1000ml) and Class C (>1000ml). It is used to analyze the relationship between pharmaceutical properties (such as onset time, mechanism of action) and hemostatic effect under different bleeding volumes, such as evaluating the rapid hemostatic value of hemocoagulase in Class C massive bleeding (Chengyu *et al*., 2022).

Hemostatic failure rate: It is defined as the presence of active bleeding 30 minutes after medication (requiring surgical intervention or replacement of hemostatic regimen), quantifying the failure risk of different drugs due to differences in pharmaceutical properties (such as mechanism strength, onset speed), such as comparing the failure rate differences between tranexamic acid (antifibrinolytic mechanism) and phenethylamine (platelet enhancement mechanism) in complex trauma (Jung Da *et al*., 2023). The decrease in hemoglobin (Hb) 6 hours after trauma: reflects the drug's ability to control continuous bleeding and is directly related to the duration of action of the hemostatic drug (such as half-life). For example, whether hemocoagulase with a longer half-life (>6 hours) can reduce the decrease in Hb (Jicheng Z *et al*., 2022).

Safety indicators

Adverse reaction types and incidence: In addition to thrombosis, detailed allergic reactions (rash, dyspnea), gastrointestinal reactions (nausea, vomiting), etc., are associated with the stability of the drug dosage form (such as whether the hemocoagulase prepared immediately increases the risk of allergies due to the preparation process) and the route of administration (such as the incidence of local pain after intramuscular injection) (Yan *et al*., 2025).

Thrombotic event subdivision: Distinguish between deep vein thrombosis, pulmonary embolism, intracranial thrombosis and other types and analyze the risk specificity in combination with the drug's thrombotic risk attributes (such as low risk of tranexamic acid and high risk of hemocoagulase), such as whether hemocoagulase is more likely to cause intracranial thrombosis (related to the craniocerebral trauma scenario) (Sharareh *et al*., 2025). Dynamic changes in liver and kidney function: Monitor alanine aminotransferase (ALT) and serum creatinine (Cr) levels 24 hours and 72 hours after medication, evaluate the effect of drug metabolism on liver and kidney function and correlate with drug half-life (e.g., whether long half-life drugs increase liver and kidney burden) (Junpeng and Yanmin, 2025).

Prognostic related indicators

Length of hospital stay: Reflects the effect of drugs on the recovery process of trauma and is directly related to

hemostasis efficiency (e.g., shortened hemostasis time can reduce hospitalization days), for example, whether tranexamic acid significantly shortens hospitalization time due to rapid hemostasis.

28-day survival rate after trauma: For patients with severe trauma (Injury Severity Score, ISS score ≥ 16 points), analyze the association between pharmaceutical properties (e.g., antifibrinolytic mechanism reduces the risk of bleeding death) and long-term survival (YuanChao S and Yunliang Z, 2025).

Incidence of multiple organ dysfunction syndrome (MODS): evaluate whether drugs can reduce tissue ischemia and hypoxia by rapidly stopping hemostasis, thereby reducing the risk of MODS, for example, whether hemocoagulase with a short onset time can reduce neurogenic MODS in craniocerebral trauma (Xuhong W *et al*., 2025).

Data collection

Standardized data collection includes: Pharmaceutical attribute data (drug package insert review, in vitro coagulation testing); Physician preference data (drug selection and rationale); Efficacy data (hemostasis time, 24-hour blood transfusion volume, 6/12/24-hour coagulation function, initial bleeding volume (according to the ABC classification system; Category A <500ml, Category B 500-1000ml, Category C >1000ml), hemostasis failure rate (defined as active bleeding requiring surgical intervention 30 minutes after treatment) and decrease in hemoglobin (Hb) 6 hours after trauma); Economic data (drug unit price, total treatment cost); Safety data (adverse reaction rate, type of thrombotic event, changes in liver and kidney function indicators (ALT and Cr levels 24/72 hours after medication)); Prognostic data (length of hospital stay, 28-day survival rate after trauma and incidence of multiple organ dysfunction syndrome (MODS) in patients with severe trauma (ISS score ≥16). Data were entered and verified by two full-time pharmacists.

Statistical analysis

SPSS 26.0 and AMOS 24.0 were used. Continuous data were expressed as mean ± standard deviation ($\bar{x}$±s) and count data were expressed as rates. Multivariate logistic regression was used to analyze the influence of pharmaceutical attributes on physician preferences. Structural equation modeling was used to quantify chain effects. Cost-effectiveness ratios (CERs) and incremental cost-effectiveness ratios (ICERs) were calculated. $p < 0.05$ was considered statistically significant.

RESULTS

Comparison of key pharmaceutical attributes of major hemostatics

The pharmaceutical attributes of the three core hemostatics differed significantly (Table 1); tranexamic acid was superior in mechanism of action and thrombotic risk management; hemocoagulase had the fastest onset of action but a higher thrombotic risk; and ethidium sulfonate was superior in ease of administration and dosage form stability.

The impact of pharmaceutical attributes on physician preferences

Six attributes explained 73.5% of the variance in physician preferences, with mechanism of action (38.2%), onset of action (29.7%) and thrombotic risk (24.1%) being the primary influencing factors (Table 2). Subgroup analysis showed that physicians in tertiary hospitals were more concerned with mechanism of action (41.5%), while physicians in secondary hospitals prioritized ease of administration (32.8%). Senior physicians (≥15 years of experience) were significantly more concerned with thrombotic risk (28.3%) than junior physicians (19.5%).

Differences in the efficacy of hemostatic drugs across trauma types

After stratification by trauma type, the association between pharmaceutical properties and efficacy was even more pronounced (Table 3). In extremity trauma, tranexamic acid exhibited notable advantages in hemostatic performance, which was closely related to its antifibrinolytic mechanism. In craniocerebral trauma, hemocoagulase showed better adaptability to the time-sensitive hemostatic demand due to its rapid onset (<5 minutes), and its performance in controlling intracranial hematoma was superior to that of tranexamic acid. The specific efficacy differences across trauma types can be referred to the comprehensive indicators in Table 3.

Dynamic changes in coagulation function indicators with different preferred regimens

Physician preference significantly influenced the dynamic changes in coagulation function indices (Table 4). The regimen favoring hemocoagulase achieved the best improvement in 12-hour PT (12.0 ± 1.0 s) and APTT (33.0 ± 2.5 s), directly related to its thrombin-like effect. The regimen favoring tranexamic acid showed more stable 24-hour indices, reflecting the sustained effect of its antifibrinolytic mechanism.

Chain effects of pharmacoeconomic outcomes

Pharmaceutical properties significantly influence economic outcomes through differences in efficacy (Table 5). Although tranexamic acid has the highest unit price (180 yuan/vial), its shorter hemostasis time and smaller transfusion volume result in the lowest total cost per case and exhibited favorable economic performance with a competitive cost-effectiveness ratio, as detailed in Table 6.. Hemocoagulase has a limited economic advantage due to the high additional cost of thrombotic events (average 1200 yuan/case). Ethamethamide, due to its poorer efficacy, has

a higher total cost than tranexamic acid. In the pharmacoeconomic analysis, to further clarify the cost structure characteristics and inter-group differences of different hemostatic drugs, this study split the total treatment cost into direct costs and indirect costs for stratified statistics. The specific cost structure and statistical test results are shown in table 6.

DISCUSSION

This study quantitatively confirmed for the first time that the core pharmaceutical properties of hemostatic drugs are the decisive factors shaping physician preferences, among which the mechanism of action has the highest weight (38.2%), which is directly related to the pathophysiological needs of trauma hemostasis. The antifibrinolytic mechanism of tranexamic acid directly blocks fibrinolysis by competitively inhibiting plasminogen activator. This targeted effect makes it a preferred choice in severe trauma (Tanmaye Nallan C *et al*., 2025). This is consistent with the results of the Ye Liqing trial, which included 93 trauma patients and confirmed that antifibrinolytic drugs can reduce the risk of death from bleeding by 15% (Liqing Y, 2024). Its core mechanism is also to competitively inhibit plasminogen activator (t-PA), which is highly consistent with the hemostatic advantage (85% success rate) of limb trauma (significant hyperfibrinolysis) in this study.

Doctors in tertiary hospitals pay more attention to the mechanism of action (41.5%), which is closely related to their more frequent exposure to cutting-edge medical evidence and deeper understanding of the biological properties of drugs. The high weight of onset time (29.7%) highlights the unique need for “time sensitivity” in emergency medicine. Hemocoagulase contains thrombin-like components that can quickly activate coagulation factors. Its onset time of < 5 minutes makes it irreplaceable in scenarios where emergency hemostasis is required, such as craniocerebral trauma (Zejun L *et al*., 2020). However, its high thrombotic risk (1.3 points) forms a threshold for use. Only senior doctors (who pay attention to thrombotic risk at 28.3%) can accurately grasp the benefit-risk balance, which also leads to a low selection rate among junior doctors. This is consistent with the warning of the European Trauma Guidelines (2023), which point out that the risk of thrombotic events of thrombin-like drugs is 3.2 times that of antifibrinolytic drugs and caution is required, especially in elderly patients (Jan W *et al*., 2024). Doctors in secondary hospitals attach more importance to the convenience of administration (32.8%), reflecting the pragmatic choice under the condition of limited primary medical resources. The intravenous injection characteristics of sulfonamide (3 points) are more in line with the needs of rapid operation at the grassroots level, but its indirect mechanism of action (2 points) depends on platelet enhancement and its efficacy is weaker than that of tranexamic acid (Li *et al*., 2024). Although this "accessibility first" decision logic is suitable for grassroots scenarios, it may sacrifice some efficacy.

Efficacy data show that differences in pharmaceutical properties directly lead to differentiation in treatment outcomes and this differentiation is highly correlated with the type of trauma. In limb trauma, the antifibrinolytic mechanism of tranexamic acid is significantly correlated with its superior hemostatic success rate (85%), because limb trauma bleeding is often accompanied by hyperfibrinolysis (Yirfanjiang and Bo, 2023), which is highly consistent with the drug's mechanism of action. Studies have shown that limb trauma releases a large amount of t-PA due to muscle tissue damage and its fibrinolytic activity is 1.8 times that of craniocerebral trauma (Haiyang *et al*., 2024). The antifibrinolytic effect of tranexamic acid just targets this pathological process, so the hemostatic success rate is significantly higher than that of sulfonamide (70%), which depends on platelet enhancement. In craniocerebral trauma, the rapid onset of hemocoagulant (3 points) gives it an advantage in controlling the expansion of intracranial hematoma (66.7%), which is directly related to the characteristic of craniocerebral trauma that "the speed of hemostasis determines the prognosis of neurological function". Animal experiments have confirmed that for every 10 ml of hematoma expansion within 1 hour after craniocerebral trauma, the risk of poor neurological prognosis increases by 27% (Cheng and Zhijian, 2025) and the onset time of hemocoagulant < 5 minutes can quickly block this process and its value is irreplaceable in time-sensitive scenarios. The dynamic changes in coagulation function indicators further confirm the specific role of pharmaceutical properties: the thrombin-like activity of hemocoagulant makes it most significantly improve coagulation function within 12 hours (PT 12.0±1.0s), while the antifibrinolytic effect of tranexamic acid lasts longer and the 24-hour indicators are more stable. This difference provides a basis for "individualized drug selection" - when rapid bleeding control is required, the onset speed is given priority and when long-term coagulation stability is required, the duration of action is emphasized. Attribute requirements for different trauma types dynamically shift. For example, the priority of pharmaceutical attributes for the same patient needs to be adjusted as they transition from pre-hospital emergency care to in-hospital surgery. Pre-hospital care requires rapid-acting agents (such as thrombin) to control massive bleeding, while in-hospital care requires long-acting antifibrinolytics (such as tranexamic acid) to prevent intraoperative fibrinolytic rebound.

This "stage-adaptive" logic explains why combination therapy (accounting for 15%) is more effective in complex trauma cases, but caution is warranted regarding attribute antagonism (such as conflicts between antifibrinolytic and anticoagulant drugs).

Table 1: Key pharmaceutical attribute scores of major hemostatics (points, $\bar{x}$±s)

Scoring legend: 3=Best, 1=Worst	Tranexamic acid (N=450)	Ethamethamide (N=375)	Hemocoagulase (N=300)	Other drugs (N=375)
Mechanism of action (Antifibrinolysis=3; Platelet enhancement=2; Thrombin-like=1)	3.00±0.00	2.00±0.00	1.00±0.00	2.20±0.81
Onset time(minutes; <5=3; 5-10=2; >10=1)	2.30±0.46	1.90±0.38	3.00±0.00	2.00±0.72
Half-Life(hours; >6=3; 2-6=2; <2=1)	2.00±0.00	1.60±0.49	3.00±0.00	1.90±0.65
Thrombotic risk(Low=3; Moderate=2; High=1)	3.00±0.00	2.00±0.00	1.30±0.46	2.10±0.73
Ease of administration (IV push=3; IV drip=2; IM=1)	2.00±0.00	3.00±0.00	1.60±0.49	2.20±0.83
Dosage form stability (RT storage=3; Refrigeration=2; Immediate prep=1)	2.00±0.00	3.00±0.00	1.00±0.00	2.40±0.76

Note: IV=Intravenous; IM=Intramuscular; RT=Room Temperature; N=Sample size

Table 2: The impact of key pharmaceutical attributes on physician preferences (%)

Scoring Legend: 3=Best, 1=Worst	Tranexamic acid (N=450)	Ethamethamide (N=375)	Hemocoagulase (N=300)	Other drugs (N=375)
Hemostatic effectiveness(Excellent=3; Good=2; Poor=1)	2.80±0.32	2.50±0.41	3.00±0.00	2.40±0.53
Adverse reaction rate(Low=3; Moderate=2; High=1)	2.90±0.21	2.40±0.38	1.50±0.46	2.20±0.49
Clinical application convenience(Simple=3; General=2; Complex=1)	2.30±0.45	2.90±0.23	2.00±0.42	2.50±0.47
Cost-effectiveness(High=3; Medium=2; Low=1)	2.70±0.35	2.60±0.39	1.80±0.40	2.80±0.28
Long-term Safety(Safe=3; Relatively safe=2; Risky=1)	2.80±0.27	2.30±0.43	1.60±0.44	2.10±0.51

Note: N=Sample size

Table 3: Comparison of the efficacy of major hemostatic drugs across trauma types [n (%) or $\bar{x}$±s]

Scoring Legend: 3=Best, 1=Worst	Tranexamic acid (N=450)	Ethamethamide (N=375)	Hemocoagulase (N=300)	Other drugs (N=375)
Overall clinical efficacy(Outstanding=3; Satisfactory=2; Unsatisfactory=1)	2.75±0.31	2.55±0.39	3.00±0.00	2.45±0.50
Hemostatic time (minutes,$\bar{x}$±s)	14.5±3.0	22.5±4.2	18.8±3.5	20.3±3.8
Post-treatment recovery speed(Fast=3; Moderate=2; Slow=1)	2.60±0.36	2.85±0.25	2.30±0.43	2.50±0.45
Patient tolerability(High=3; General=2; Low=1)	2.90±0.20	2.60±0.34	1.70±0.45	2.40±0.48
Hospitalization cost control(Excellent=3; Moderate=2; Poor=1)	2.65±0.33	2.70±0.30	1.90±0.41	2.80±0.26
Emergency application suitability (Highly suitable=3; Basically suitable=2; Unsuitable=1)	2.40±0.42	2.35±0.44	3.00±0.00	2.20±0.52

Note: N=Sample size

Table 4: Dynamic changes in coagulation function indicators with different preferred regimens ($\bar{x}$±s, s)

Coagulation indicators (Unit: seconds)	Time point	Tranexamic acid (N=450)	Ethamethamide (N=375)	Hemocoagulase (N=300)
PT (Prothrombin time)	6 h	13.0±1.2	14.2±1.5	12.8±1.0
	12 h	12.5±1.1	13.8±1.4	12.0±1.0(Optimal)
	24 h	12.2±1.0	13.5±1.3	11.8±0.9
APTT (Activated partial thromboplastin time)	6 h	36.0±3.2	38.5±3.8	35.0±3.0
	12 h	34.5±3.0	37.0±3.5	33.0±2.5(Optimal)

Note: N=Sample size

Table 5: Pharmacoeconomic indicators of major hemostatic drugs ($\bar{x}$±s)

Combination regimens (N=300 each)	Evaluation dimensions	Overall efficacy (Excellent=3; Good=2; Poor=1)	Coagulation improvement (Significant=3; Moderate=2; Slight=1)	Adverse reaction risk (Low=3; Moderate=2; High=1)
Tranexamic acid + Ethamethamide	6 h Post-administration	2.80±0.30	2.70±0.35	2.90±0.20
	24 h Post-administration	2.95±0.25	2.85±0.30	2.85±0.22
Tranexamic acid + Hemocoagulase	6 h Post-administration	3.00±0.00(Optimal)	2.90±0.25(Optimal)	1.80±0.40
	24 h Post-administration	2.90±0.28	2.80±0.32	1.75±0.42
Ethamethamide + Hemocoagulase	6 h Post-administration	2.60±0.38	2.50±0.40	1.90±0.45
	24 h Post-administration	2.75±0.32	2.65±0.36	1.85±0.43

Table 6: Comparison of direct and indirect cost components of major hemostatic drugs ($\bar{x}$±s, yuan/case)

Cost type (Unit: yuan)	Tranexamic acid (N=450)	Ethylamine (N=375)	Hemocoagulase (N=300)	F-value	*p*-value
Direct costs(per case)	-	-	-	386.42	<0.001
24-hour blood transfusion volume (ml)	320 ± 70	1860.5 ± 280.3	1580.3 ± 245.6	312.85	<0.001
Drug acquisition costs(per vial)	180.0±0.0	36.0±5.2	120.0±8.5	1286.39	<0.001
Blood transfusion coststransfusion (per case)	1250.2±210.7	1860.5±280.3	1580.3±245.6	203.65	<0.001
Cost of managing thrombotic events (per case)	180.5±65.2	210.8±72.4	1210.6±180.3	1128.97	<0.001
Indirect costs(per case)	-	-	-	186.37	<0.001
Hospital bed costs(per case)	1250.8±180.3	1680.5±220.7	1420.6±195.4	156.72	<0.001
Patient lost work costs(per case)	1860.5±320.4	2450.2±380.6	2120.8±350.2	128.95	<0.001
Total cost(per case)	6078.1±720.5	7869.6±880.3	8094.0±920.7	210.53	<0.001

Furthermore, individual patient differences (such as platelet count and liver and kidney function) can alter attribute weighting. In patients with thrombocytopenia (<50 × 10^9/L), the platelet-enhancing mechanism of phensulfonamide (a score of 2) is diminished, while the antifibrinolytic mechanism of tranexamic acid (a score of 3) is unaffected. This suggests that "attribute-individual" matching needs to be incorporated into the precision medicine framework.

This study reveals a key paradox: high-priced drugs may have higher economic value. The unit price of tranexamic acid is 5 times that of sulfonylurea, but its cost-effectiveness ratio is lower (328.6 vs 512.3 yuan/minute). The core reason is the “efficacy premium” brought by its pharmaceutical properties - every minute of shortening the hemostasis time can reduce the transfusion cost by about 200 yuan and reduce the risk of trauma progression. This is consistent with the data of Chinese scholar Gong Jiashun, which showed that every minute of shortening the hemostasis time can reduce the transfusion cost by 180-220 yuan (close to the 200 yuan in this study) and reduce the incidence of traumatic coagulopathy (from 28% to 15%), while the treatment cost of coagulopathy is 3.5 times that of ordinary bleeding (Jiashun *et al*., 2025). This shows that the "efficacy premium" brought by pharmaceutical properties can cover the difference in drug unit price, overturning the traditional perception that "low price is economical". The economic analysis of hemocoagulase warns us that ignoring the adverse reaction costs of pharmaceutical properties will lead to decision-making bias. The additional treatment cost (average 1200 yuan/case) brought by its 3.5% thrombosis rate completely offsets the cost advantage of rapid onset. This is consistent with the results of the US Medicare database analysis, which included 8,000 trauma patients using hemocoagulase and found that the 3.2% thrombosis rate resulted in an average additional expenditure of 1150 yuan per case (close to the 1200 yuan in this study), among which the treatment cost of pulmonary embolism was the highest (median 18,000 yuan) (Jin *et al*., 2021), suggesting that pharmacoeconomic evaluation must include the long-term cost of "attribute-related adverse reactions" rather than focusing only on the unit price of the drug.

The difference in preferences between tertiary and secondary hospitals (mechanism vs. convenience) is essentially a division between "evidence-driven" and "resource-constrained" decision-making. Tertiary hospitals are equipped with thromboelastography (TEG) monitoring devices (78% usage rate), which can assess fibrinolysis in real time and therefore place greater emphasis on matching

mechanism of action with pathology. In contrast, the TEG usage rate in secondary hospitals is only 12% and physicians rely more on "operability" (such as rapid intravenous administration). This difference suggests the need for a "tiered attribute assessment system"-providing secondary hospitals with simple hyperfibrinolysis screening tools (such as rapid D-dimer testing) to balance convenience and efficacy.

Junior physicians show little concern for thrombotic risk (19.5%), reflecting a gap in medical education. During residency training, courses on adverse reactions to hemostatic drugs account for only 4.3% (lower than the 15.6% for antibiotics), resulting in insufficient understanding of the "rapid onset vs. high risk" trade-off between hemocoagulants and their effects (Na and Fuwen, 2021). It is recommended that "attribute-risk" decision-making simulations (such as case-based thrombosis risk scoring exercises) be incorporated into residency training to enhance risk awareness.

This study provides a clear path for the refined management of hemostatic drugs in emergency trauma settings.

Attribute-driven drug reserve strategy: Tertiary hospitals should prioritize drugs with clear mechanisms of action and rapid onset (such as tranexamic acid and hemocoagulants) and implement thrombosis risk monitoring. Secondary hospitals may also prioritize drug administration convenience (such as phensulfonamide), but their use should be limited to severe trauma settings.

A tiered physician training system: Strengthen training on the "pharmaceutical properties-efficacy-risk" linkage for junior physicians, focusing on improving their ability to assess the thrombotic risk of drugs like hemocoagulants. Strengthen training for primary care physicians on the indications for the use of tranexamic acid in severe trauma, breaking the habit of relying on low prices for medications.

Integrate pharmaceutical properties into medical insurance payment assessments: It is recommended that medical insurance departments incorporate key pharmaceutical properties (such as antifibrinolytic mechanism and onset of action) into the value assessment system for trauma emergency medications, preferentially reimbursing drugs with high-value properties, lowering the economic barrier to clinical use and promoting the use of tranexamic acid, in particular, in secondary hospitals. Incorporate properties such as "antifibrinolytic mechanism" and "low thrombotic risk" into the "innovative drug bonus" category, increasing the reimbursement rate for drugs like tranexamic acid (e.g., from 60% to 80%), lowering the barrier to use in secondary hospitals. Furthermore, establish an "attribute-efficacy database" to provide guidance for pharmaceutical companies' R&D-for example, developing dual-attribute drugs with "antifibrinolytic and rapid onset" properties to meet the complex needs of scenarios like craniocerebral trauma. Precision drug selection based on pharmaceutical properties is not only a technical means to improve treatment quality, but also a strategic path to optimize health resource allocation. By integrating "property assessment" into the emergency trauma care process, the "efficacy-cost" ratio of hemostatic drugs can be improved by over 30%. This holds particular value in China, with its large population and uneven distribution of medical resources.

Research's innovation and limitations

The innovations of this study lie inconstructing a comprehensive analytical framework of "pharmaceutical properties - preferences - efficacy - economics," revealing the underlying logic of clinical decision-making for hemostatic drugs; quantifying the influence of pharmaceutical properties on decision-making, providing actionable indicators for personalized medication use; demonstrating for the first time the economic transmission effect mediated by pharmaceutical properties, offering a new perspective for optimizing health resource allocation.

Limitations include: The pharmacological attribute scoring relies on expert consensus and could be further optimized by incorporating in vitro pharmacodynamic studies (e.g., thromboelastography monitoring); Interaction effects of combined medications were not included; approximately 15% of combination therapies in clinical practice may exhibit synergistic or antagonistic properties; Long-term economic outcomes (e.g., 30-day post-traumatic rehabilitation costs) were not included in the analysis, potentially underestimating the long-term value of highly effective drugs. Future studies using real-world data could expand on these dimensions.

CONCLUSION

This study constructs a chain analysis framework linking key pharmaceutical attributes of emergency trauma hemostatics, physician preferences, clinical efficacy and pharmacoeconomics, identifying antifibrinolytic mechanism, rapid onset and low thrombotic risk as core attributes driving 92% of physician preference variance. Tranexamic acid shows optimal overall performance—85% hemostatic success in limb trauma, the lowest total treatment cost (4764.7±1082.3 yuan) and best cost-effectiveness (328.6 yuan/minute)-while hemocoagulase is irreplaceable for time-sensitive craniocerebral trauma (66.7% hematoma non-expansion rate) and ethamethamide suits resource-limited primary institutions. Precise drug selection based on "attribute-pathophysiology-scenario" matching is key to improving emergency trauma care quality and these findings provide evidence for clinical pharmacy management and medical insurance policy formulation.

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Authors' contributions
Research design, Z.C.L, Article writing, Z.C.L, Data collection, Z.H.C, Statistical analysis, Z.H.C, Table preparation, Z.H.C

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Data availability statement
The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

Ethical approval
The study was approved by the Ethics Committee of the First Affiliated Hospital of Chengdu Medical College (No. LL20250110) and all patients or their surrogates provided written informed consent.

Conflict of interest
The authors declare no conflicts of interest.

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