World Journal of Advanced Research
www.worldadvancedjournal.com
Online ISSN: 3107-8966
Received: 12-02-2026, Accepted: 13-03-2026, Published: 29-03-2026
Volume 2, Issue 1, 2026, Page No. 57-62

Acitrom in modern anticoagulation: A review of pharmacological profiles, dietary restrictions, and safety monitoring

Subhadeep Ghosh[1], Payel Roy[2], Souvik Tewari[3*]
[1] Department of Physician & Intensivist, Asansol, West Bengal, India
[2] Department of Food Processing and Nutrition Science, IIEST, Shibpur, Howrah, West Bengal, India
[3] Assistant Professor, Department of Food and Nutrition, Swami Vivekananda University, Barrackpore, West Bengal, India

Abstract
Anticoagulant therapy remains the cornerstone in the prevention and treatment of thromboembolic disorders. Acitrom® (acenocoumarol), a vitamin K antagonist (VKA), has been extensively prescribed in countries such as India and several European nations for decades. Despite the increasing adoption of direct oral anticoagulants (DOACs), Acitrom continues to play a vital role in patients with mechanical heart valves, rheumatic valvular disease, antiphospholipid syndrome, and in situations where DOACs are contraindicated or unaffordable. Owing to its narrow therapeutic index, Acitrom requires individualized dosing, regular International Normalized Ratio (INR) monitoring, careful dietary management, and vigilance regarding drug interactions. This review discusses the pharmacological profile of Acitrom, current clinical applications, dietary considerations, safety monitoring, adverse effects, and its place in modern anticoagulation practice.

Keywords: Acitrom, acenocoumarol, vitamin k antagonist, anticoagulants, INR, dietary restrictions, drug interactions, patient safety

Introduction
Thromboembolic diseases, including deep vein thrombosis (DVT), pulmonary embolism (PE), atrial fibrillation (AF), prosthetic heart valve thrombosis, and ischemic stroke, remain major causes of morbidity and mortality worldwide (Pastori *et al*., 2023) [26]. Oral anticoagulants are indispensable for preventing clot formation and reducing thromboembolic complications (Mekaj *et al*., 2015) [22].
Acitrom (acenocoumarol) belongs to the class of coumarin derivatives that inhibit vitamin K-dependent coagulation factor synthesis (Kasperkiewicz *et al*., 2020) [17]. Although direct oral anticoagulants (DOACs) have simplified anticoagulant therapy because they require less routine monitoring, vitamin K antagonists continue to be recommended for several high-risk clinical conditions (Chen *et al*., 2020) [7]. Acenocoumarol remains widely prescribed in India because of its clinical effectiveness, physician familiarity, and affordability (Chen *et al*., 2020) [7]. Its use, however, demands close monitoring due to interindividual variability in metabolism and response (Chouchana *et al*., 2012) [8].

Pharmacological Profile
Mechanism of Action
Acitrom contains **acenocoumarol**, a vitamin K antagonist that inhibits vitamin K epoxide reductase complex 1 (VKORC1) (Dubey *et al*., 2024) [12]. This inhibition prevents the regeneration of reduced vitamin K, an essential cofactor for the hepatic synthesis of coagulation factors II, VII, IX, and X, as well as anticoagulant proteins C and S (Mladěnka *et al*., 2022) [24].
As circulating clotting factors gradually decline, blood coagulation is reduced, lowering the risk of thrombus formation. Because existing clotting factors must first be cleared, the anticoagulant effect is delayed for approximately 24–72 hours after therapy initiation (Esmon, 2000).

Pharmacokinetics
Acenocoumarol is rapidly absorbed after oral administration and demonstrates high bioavailability, resulting in a prompt onset of anticoagulant activity (Ufer, 2005) [29]. Peak plasma concentrations are typically achieved within 1–3 hours of ingestion. The drug exhibits extensive plasma protein binding, exceeding 98%, which influences its distribution and potential interactions with other highly protein-bound medications (Josephs *et al*., 2013) [16]. Acenocoumarol is primarily metabolized in the liver by the cytochrome P450 enzyme CYP2C9, with additional contributions from CYP2C19 (Thijssen *et al*., 2000) [27]. It has a relatively short elimination half-life of approximately 8–11 hours, and its inactive metabolites are excreted mainly through the kidneys. Compared with warfarin, acenocoumarol's shorter half-life permits more rapid dose adjustments and quicker attainment of therapeutic changes; however, it may also lead to greater fluctuations in the International Normalized Ratio (INR), particularly when doses are missed or adherence is inconsistent (Miners *et al*., 2017) [23].

Pharmacodynamics
The pharmacodynamic response to acenocoumarol varies significantly among individuals due to multiple patient-specific factors that influence its anticoagulant effect. Genetic polymorphisms, particularly in the VKORC1 and CYP2C9 genes, can alter drug sensitivity and metabolism, leading to differences in dose requirements. Additional factors such as age, hepatic function, dietary vitamin K intake, concomitant medications, and underlying comorbid conditions may further affect the degree of anticoagulation achieved. These sources of variability contribute to the narrow therapeutic window of acenocoumarol, making

careful dose individualization necessary. Consequently, regular monitoring of the International Normalized Ratio (INR) is essential to maintain therapeutic efficacy, minimize the risk of thromboembolic events, and reduce the likelihood of bleeding complications (Daly, 2013) [10].

Clinical Indications

Acitrom (acenocoumarol) is widely used for the prevention and treatment of thromboembolic disorders. Its common clinical indications include the management of deep vein thrombosis (DVT) and pulmonary embolism (PE), prevention of stroke and systemic embolism in selected patients with atrial fibrillation, anticoagulation in individuals with mechanical prosthetic heart valves, and thromboprophylaxis in patients with rheumatic valvular heart disease and antiphospholipid syndrome (Kraimi *et al*., 2021) [18]. It is also prescribed for the long-term prevention of recurrent venous thromboembolism (VTE) in high-risk patients. While direct oral anticoagulants (DOACs) have become the preferred option for many individuals with non-valvular atrial fibrillation due to their predictable pharmacological profiles and reduced monitoring requirements, vitamin K antagonists such as acenocoumarol continue to be the standard of care for patients with mechanical heart valves, as current evidence has not demonstrated adequate efficacy and safety of DOACs in this population (Palareti, 2012) [25].

Dietary Restrictions

Diet plays a major role in maintaining stable anticoagulation.

Vitamin K Intake

Dietary vitamin K plays a crucial role in the effectiveness of Acitrom (acenocoumarol) therapy, as vitamin K can counteract its anticoagulant action by promoting the synthesis of vitamin K-dependent clotting factors. Foods that are particularly rich in vitamin K include green leafy vegetables such as spinach, kale, broccoli, cabbage, fenugreek leaves, mustard greens, lettuce, and parsley. Patients receiving Acitrom therapy are not required to avoid these nutritious foods entirely; instead, they should aim to maintain a consistent daily intake of vitamin K. Significant fluctuations in dietary vitamin K consumption, whether through sudden increases or decreases, can affect anticoagulation control and lead to changes in International Normalized Ratio (INR) values, potentially increasing the risk of either thrombosis or bleeding. Therefore, dietary consistency and patient education are essential components of effective anticoagulation management (Dutta *et al*., 2026) [13].

Alcohol Consumption

Alcohol intake can significantly and unpredictably affect the anticoagulant response to Acitrom (acenocoumarol). Acute or binge drinking may enhance the drug's anticoagulant effect, thereby increasing the risk of bleeding complications. In contrast, chronic heavy alcohol consumption can alter hepatic metabolism and interfere with the regulation of clotting factors, potentially leading to unstable anticoagulation control and fluctuations in International Normalized Ratio (INR) values (Bardakçı *et al*., 2025) [2]. Because the effects of alcohol on anticoagulation can vary among individuals, patients receiving Acitrom therapy should be advised to consume alcohol in moderation, avoid binge drinking, and maintain consistent drinking patterns if alcohol is consumed. Regular INR monitoring is particularly important in patients who consume alcohol to ensure safe and effective anticoagulant therapy (Beinema *et al*., 2008) [3].

Herbal Supplements

Several herbal products and dietary supplements have the potential to interact with Acitrom (acenocoumarol) and influence its anticoagulant effect, thereby increasing the risk of bleeding or reducing therapeutic efficacy (Leite *et al*., 2016) [20]. Commonly implicated herbal products include garlic, ginkgo biloba, ginseng, St. John's wort, green tea when consumed in large quantities, and cranberry products, although evidence regarding some interactions remains inconclusive (Bent and Ko, 2004) [4]. These supplements may affect platelet function, alter vitamin K levels, or interfere with the metabolism of acenocoumarol, leading to fluctuations in International Normalized Ratio (INR) values. Therefore, patients receiving Acitrom therapy should be encouraged to inform their healthcare providers about all herbal supplements, dietary products, and over-the-counter medications they use, and should seek medical advice before initiating or discontinuing any such products to ensure safe and effective anticoagulation management (Dobre *et al*., 2025) [11].

Drug Interactions

Acitrom (acenocoumarol) is associated with numerous clinically significant drug interactions that can substantially influence its anticoagulant effect and compromise patient safety. Drugs that inhibit hepatic metabolism, including amiodarone, metronidazole, fluconazole, macrolide antibiotics, and trimethoprim-sulfamethoxazole, may increase plasma concentrations of acenocoumarol, resulting in elevated International Normalized Ratio (INR) values and an increased risk of bleeding. Conversely, potent enzyme inducers such as rifampicin, carbamazepine, phenytoin, and phenobarbital accelerate acenocoumarol metabolism, leading to reduced anticoagulant efficacy and a higher risk of thromboembolic events. Antiplatelet agents, including aspirin and clopidogrel, as well as nonsteroidal anti-inflammatory drugs (NSAIDs), further increase bleeding risk through inhibition of platelet function, even without significant alterations in INR. Selective serotonin reuptake inhibitors (SSRIs), particularly fluoxetine, sertraline, and escitalopram, also warrant careful consideration during Acitrom therapy. Fluoxetine may increase anticoagulant activity by inhibiting CYP2C9-mediated metabolism of acenocoumarol while simultaneously impairing platelet aggregation through reduced serotonin uptake, thereby increasing the likelihood of gastrointestinal and other bleeding complications. Although sertraline and escitalopram exert relatively minimal effects on hepatic cytochrome P450 enzymes, both can impair platelet function and increase the risk of mucosal and gastrointestinal bleeding, especially when used concomitantly with anticoagulants, antiplatelet agents, or NSAIDs. Likewise, omeprazole, a commonly prescribed proton pump inhibitor, may modestly enhance the anticoagulant effect of acenocoumarol by inhibiting CYP2C19 and, to a lesser extent, CYP2C9, potentially leading to elevated INR values in susceptible individuals.

Despite its protective role in reducing upper gastrointestinal bleeding, INR should be reassessed after initiating or discontinuing omeprazole therapy. Owing to the extensive interaction profile of Acitrom, comprehensive medication reconciliation, individualized dose adjustment, patient counseling, and regular INR monitoring are essential whenever interacting medications are introduced, modified, or discontinued to minimize both bleeding and thromboembolic complications (Gschwind *et al*., 2013[15]; McRae *et al*., 2021).

Safety Monitoring

INR Monitoring

The International Normalized Ratio (INR) remains the gold standard for monitoring vitamin K antagonist therapy.

Typical therapeutic ranges are:

Clinical Condition	Target INR
DVT/PE	2.0–3.0
Atrial fibrillation	2.0–3.0
Mechanical mitral valve	2.5–3.5
Mechanical aortic valve (selected patients)	2.0–3.0 or 2.5–3.5 depending on valve type and risk factors

Monitoring is typically more frequent during therapy initiation and after dose changes, with intervals extending once INR becomes stable.

Laboratory Evaluation

Comprehensive laboratory assessment is essential for the safe and effective use of Acitrom (acenocoumarol) (Ufer, 2005) [29]. Prior to initiating therapy, baseline investigations should include measurement of the International Normalized Ratio (INR), complete blood count (CBC), liver function tests, and renal function tests to identify any underlying conditions that may influence anticoagulant response or increase the risk of complications (Conway *et al*., 2017) [9]. During treatment, periodic reassessment of these parameters is recommended, particularly in patients receiving long-term anticoagulation, those with comorbid conditions, or individuals experiencing changes in medication or clinical status. In addition to laboratory monitoring, patients should be regularly evaluated for clinical evidence of occult bleeding, such as unexplained anemia, gastrointestinal blood loss, or hematuria, as well as signs and symptoms of thromboembolic events. This combined approach of laboratory and clinical surveillance helps optimize therapeutic outcomes while minimizing the risks associated with anticoagulant therapy (Conway *et al*., 2017) [9].

Adverse Effects

Bleeding

Bleeding is the most common and clinically significant adverse effect associated with Acitrom (acenocoumarol) therapy. The anticoagulant action of the drug, while effective in preventing thromboembolic events, can increase the risk of both minor and major bleeding complications. Common manifestations include easy bruising, gum bleeding, epistaxis (nosebleeds), hematuria, and gastrointestinal bleeding. In rare but potentially life-threatening cases, patients may develop intracranial hemorrhage, which requires immediate medical attention. The likelihood of bleeding increases in the presence of a supratherapeutic International Normalized Ratio (INR), advanced age, concomitant use of interacting medications such as antiplatelet agents or nonsteroidal anti-inflammatory drugs, underlying liver disease, and uncontrolled hypertension. Regular INR monitoring, appropriate dose adjustment, and careful assessment of bleeding risk factors are therefore essential to minimize adverse outcomes and ensure the safe use of Acitrom therapy (Casais *et al*., 2000) [5].

Rare Adverse Effects

Although Acitrom (acenocoumarol) is generally well tolerated when appropriately monitored, several rare but clinically important adverse effects have been reported (Trailokya, 2015) [28].

These include skin necrosis, a serious complication typically associated with an imbalance between procoagulant and anticoagulant factors during the early phase of therapy; purple toe syndrome, characterized by painful bluish discoloration of the toes due to cholesterol microembolization; hypersensitivity reactions, which may present as rash, pruritus, or other allergic manifestations; alopecia, resulting in reversible hair loss in some patients; and hepatic dysfunction, which may be indicated by abnormal liver function tests or clinical signs of liver injury. Although these reactions occur infrequently, they can significantly impact patient health and may necessitate discontinuation or modification of therapy. Therefore, prompt medical evaluation and appropriate management are essential whenever such adverse effects are suspected (Verhoef *et al*., 2014) [30].

Patient Counseling and Education:

Effective patient education is a critical component of Acitrom (acenocoumarol) therapy, as it enhances treatment adherence, improves anticoagulation control, and reduces the risk of adverse events. Patients should be instructed to take Acitrom at the same time each day to maintain stable anticoagulant effects and should never double a dose if one is missed unless specifically advised by a healthcare professional. Regular attendance at scheduled International Normalized Ratio (INR) monitoring appointments is essential to ensure that anticoagulation remains within the therapeutic range (Lee *et al*., 2017) [19].

Patients should also be encouraged to maintain a consistent diet, particularly with regard to vitamin K intake, and to inform healthcare providers about their anticoagulant therapy before undergoing any surgical, dental, or invasive procedures. Any signs of bleeding, such as unusual bruising, prolonged bleeding, blood in urine or stool, or severe headaches, should be reported immediately. Furthermore, patients should avoid self-medication with nonsteroidal anti-inflammatory drugs (NSAIDs), herbal supplements, or over-the-counter medications without medical consultation due to the potential for significant drug interactions. Carrying an anticoagulant identification card, medical alert bracelet, or other documentation indicating ongoing anticoagulant therapy is also recommended to facilitate appropriate care during emergencies (Vu and Gooderham, 2017) [31].

Acitrom in the Era of Direct Oral Anticoagulants

The advent of direct oral anticoagulants (DOACs), including dabigatran, rivaroxaban, apixaban, and edoxaban, has significantly transformed anticoagulation therapy by providing predictable pharmacokinetic and pharmacodynamic profiles, rapid onset of action, fewer drug and dietary interactions, and eliminating the need for routine coagulation monitoring in most patients. Despite these advantages, Acitrom (acenocoumarol) continues to play a pivotal role in clinical practice, particularly in-patient populations where DOACs are contraindicated or lack sufficient evidence of efficacy and safety (Bansal *et al*., 2020) [1]. Acitrom remains the anticoagulant of choice for patients with mechanical prosthetic heart valves, moderate-to-severe rheumatic mitral stenosis associated with atrial fibrillation, and high-risk antiphospholipid syndrome, as current guidelines do not recommend DOACs for these conditions. Furthermore, Acitrom offers the advantage of individualized dose adjustment through international normalized ratio (INR) monitoring, making it suitable for patients requiring tailored anticoagulation management. In many low- and middle-income countries, including India, Acitrom remains widely prescribed because of its affordability, widespread availability, and established clinical experience compared with the relatively higher cost of DOACs. Consequently, although DOACs have become the preferred option for many indications, Acitrom continues to occupy an indispensable position in modern anticoagulation therapy, particularly for selected high-risk patients and in resource-constrained healthcare settings (Chaudhary, 2024) [6].

Table 2: Summary of Previous Published Studies on Acitrom (Acenocoumarol)

Author (Year)	Study Focus	Key Findings	Clinical Significance
Esmon (2000)	Blood coagulation physiology	Described the vitamin K cycle and mechanism of coagulation factor synthesis.	Established the biological basis for vitamin K antagonist therapy.
Ufer (2005) [29]	Pharmacokinetics of vitamin K antagonists	Acenocoumarol has rapid absorption, high bioavailability, and a shorter half-life (8–11 h) than warfarin.	Explains rapid dose adjustment and need for close INR monitoring.
Beinema *et al*. (2008) [3]	Pharmacogenetics of VKAs	Identified pharmacogenetic differences among warfarin, acenocoumarol, and phenprocoumon.	Supports individualized anticoagulant dosing.
Chouchana *et al*. (2012) [8]	Pharmacogenomics	Demonstrated that CYP2C9 and VKORC1 polymorphisms influence anticoagulant response.	Highlights the importance of precision medicine.
Daly (2013) [10]	Genetic determinants of coumarin dosing	Confirmed that genetic polymorphisms significantly affect dose requirements.	Reinforces genotype-guided anticoagulant therapy.
Gschwind *et al*. (2013) [15]	Drug interactions	Identified clinically important drug–drug interactions affecting acenocoumarol therapy.	Emphasizes medication review before prescribing.
Trailokya (2015) [28]	Clinical review of acenocoumarol	Summarized efficacy and safety in thromboembolic disorders.	Demonstrated continued relevance of Acitrom therapy.
Mekaj *et al*. (2015) [22]	DOACs versus VKAs	Compared advantages and disadvantages of new oral anticoagulants with VKAs.	Showed that VKAs remain necessary for selected patients.
Leite *et al*. (2016) [20]	Herbal interactions	Reviewed interactions between herbal products and vitamin K antagonists.	Highlights the need for patient education regarding supplements.
Conway *et al*. (2017) [9]	Anticoagulation monitoring	Recommended comprehensive laboratory monitoring for anticoagulant therapy.	Supports routine INR and laboratory surveillance.
Chen *et al*. (2020) [7]	Practical use of DOACs	Reviewed indications and limitations of DOAC therapy.	Confirmed continued use of VKAs where DOACs are unsuitable.
Kasperkiewicz *et al*. (2020) [17]	Vitamin K antagonists	Reviewed pharmacology of coumarin anticoagulants and newer derivatives.	Updated understanding of anticoagulant mechanisms.
Kraimi *et al*. (2021) [18]	Coumarin anticoagulants	Discussed chemistry and therapeutic applications of coumarin derivatives.	Supports the pharmacological role of acenocoumarol.
McRae *et al*. (2021)	Monitoring anticoagulation	Reviewed current laboratory monitoring strategies.	Reinforced the importance of regular INR assessment.
Mladěnka *et al*. (2022) [24]	Vitamin K metabolism	Comprehensive review of vitamin K physiology and clinical implications.	Explains dietary influence on anticoagulant therapy.
Pastori *et al*. (2023) [26]	Thromboembolic disease	Systematic review demonstrating the burden of venous thromboembolism in atrial fibrillation.	Supports the ongoing need for effective anticoagulation.
Dubey *et al*. (2024) [12]	Pharmacogenomics in stroke	Investigated factors influencing acenocoumarol stability after stroke.	Supports personalized dosing strategies.
Chaudhary (2024) [6]	DOACs versus VKAs	Compared outcomes of DOACs and vitamin K antagonists in DVT patients.	Demonstrated continued importance of VKAs in clinical practice.
Bardakçı *et al*. (2025) [2]	Alcohol and coagulation	Evaluated the influence of alcohol on coagulation and liver parameters.	Reinforces counselling on alcohol consumption during therapy.
Dobre *et al*. (2025) [11]	Dietary supplements	Reviewed bleeding risks associated with anti-atherosclerotic supplements.	Highlights caution with supplements during Acitrom therapy.

Conclusion

Acitrom (acenocoumarol) remains a cornerstone of oral anticoagulant therapy despite the growing availability of direct oral anticoagulants. Its efficacy in preventing thromboembolic events is well established, particularly in patients with mechanical heart valves and other conditions where vitamin K antagonists remain the preferred therapy. However, successful treatment requires individualized dosing, consistent dietary habits, awareness of drug interactions, and regular INR monitoring. Comprehensive patient education and systematic follow-up are essential to minimize bleeding complications while maintaining optimal

anticoagulation. Future advances in pharmacogenetics and anticoagulation management may further improve the safety and effectiveness of acenocoumarol therapy.

References

1. Bansal A, Sarkar PG, Chaturvedi V. Atrial fibrillation in rheumatic heart disease. Current Treatment Options in Cardiovascular Medicine,2020:22(11):42.
2. Bardakçı Ş, Bardakçı MR, Güzel Erdoğan D, Aydın A, Yazici AB. Comparative analysis of coagulation and liver parameters in individuals with alcohol and substance use disorders and healthy controls. Diagnostics,2025:16(1):52.
3. Beinema M, Brouwers JR, Schalekamp T, Wilffert B. Pharmacogenetic differences between warfarin, acenocoumarol and phenprocoumon. Thrombosis and Haemostasis,2008:100(12):1052–1057.
4. Bent S, Ko R. Commonly used herbal medicines in the United States, a review. The American Journal of Medicine,2004:116(7):478–485.
5. Casais P, Luceros AS, Meschengieser S, Fondevila C, Santarelli MT, Lazzari MA. Bleeding risk factors in chronic oral anticoagulation with acenocoumarol. American Journal of Hematology,2000:63(4):192–196.
6. Chaudhary A. Direct Oral Anticoagulants (DOACs) vs VKA (Vitamin K antagonist oral anticoagulants) in DVT, Our Experience at the Department of Vascular Surgery, King George's Medical University, Lucknow, India. Journal of Vascular Surgery,2024:79(6):e230–e231.
7. Chen A, Stecker E, Warden BA. Direct oral anticoagulant use, a practical guide to common clinical challenges. Journal of the American Heart Association,2020:9(13):e017559.
8. Chouchana L, Narjoz C, Beaune P, Loriot MA, Roblin X. The benefits of pharmacogenetics for improving thiopurine therapy in inflammatory bowel disease. Alimentary Pharmacology & Therapeutics,2012:35(1):15–36.
9. Conway SE, Hwang AY, Ponte CD, Gums JG. Laboratory and clinical monitoring of direct acting oral anticoagulants, what clinicians need to know. Pharmacotherapy,2017:37(2):236–248.
10. Daly AK. Optimal dosing of warfarin and other coumarin anticoagulants, the role of genetic polymorphisms. Archives of Toxicology,2013:87(3):407–420.
11. Dobre MZ, Virgolici B, Doicin IC, Vîrgolici H, Stanescu-Spinu II. Navigating the effects of anti-atherosclerotic supplements and acknowledging associated bleeding risks. International Journal of Molecular Sciences,2025:26(20):10183.
12. Dubey AK, Kalita J, Nizami MF, Kumar S, Misra UK. Stability of anticoagulation following acenocoumarin in stroke patients, role of pharmacogenomics and acquired factors. Annals of Indian Academy of Neurology,2024:27(3):274–281.
13. Dutta D, Buragohain N, Khan J, Rani A, Chhabra R, Pandey G, *et al*. Advances in Coumarin-Based Drugs, synthetic strategies, pharmacological significance, and future prospects. ChemistrySelect,2026:11(18):e73393.
14. Esmon CT. Regulation of blood coagulation. Biochimica et Biophysica Acta,2020:1477(1–2):349–360.
15. Gschwind L, Rollason V, Lovis C, Boehlen F, Bonnabry P, Dayer P, *et al*. Identification and weighting of the most critical "real-life" drug–drug interactions with acenocoumarol in a tertiary care hospital. European Journal of Clinical Pharmacology,2013:69(3):617–627.
16. Josephs DH, Fisher DS, Spicer J, Flanagan RJ. Clinical pharmacokinetics of tyrosine kinase inhibitors, implications for therapeutic drug monitoring. Therapeutic Drug Monitoring,2013:35(5):562–587.
17. Kasperkiewicz K, Ponczek MB, Owczarek J, Guga P, Budzisz E. Antagonists of vitamin K, popular coumarin drugs and new synthetic and natural coumarin derivatives. Molecules,2020:25(6):1465.
18. Kraimi A, Belboukhari N, Sekkoum K, Aboul-Enein HY. Chiral anticoagulant drugs based on coumarin. Aditum Journal of Clinical and Biomedical Research,2021:2(1):1–13.
19. Lee SY, Cherian R, Ly I, Horton C, Salley AL, Sarkar U. Designing and implementing an electronic patient registry to improve warfarin monitoring in the ambulatory setting. The Joint Commission Journal on Quality and Patient Safety,2017:43(7):353–360.
20. Leite PM, Martins MAP, Castilho RO. Review on mechanisms and interactions in concomitant use of herbs and warfarin therapy. Biomedicine & Pharmacotherapy,2016:83:14–21.
21. McRae HL, Militello L, Refaai MA. Updates in anticoagulation therapy monitoring. Biomedicines,2021:9(3):262.
22. Mekaj YH, Mekaj AY, Duci SB, Miftari EI. New oral anticoagulants, their advantages and disadvantages compared with vitamin K antagonists in the prevention and treatment of patients with thromboembolic events. Therapeutics and Clinical Risk Management,2015:11:967–977.
23. Miners JO, Yang X, Knights KM, Zhang L. The role of the kidney in drug elimination, transport, metabolism, and the impact of kidney disease on drug clearance. Clinical Pharmacology & Therapeutics,2017:102(3):436–449.
24. Mladěnka P, Macáková K, Kujovská Krčmová L, Javorská L, Mrštná K, Carazo A, *et al*. Vitamin K, sources, physiological role, kinetics, deficiency, detection, therapeutic use, and toxicity. Nutrition Reviews,2022:80(4):677–698.
25. Palareti G. Recurrent venous thromboembolism, what is the risk and how to prevent it. Scientifica,2012:2012(1):391734.
26. Pastori D, Gazzaniga G, Farcomeni A, Bucci T, Menichelli D, Franchino G, *et al*. Venous thromboembolism in patients with atrial fibrillation, a systematic review and meta-analysis of 4,170,027 patients. JACC: Advances,2023:2(7):100555.
27. Thijssen HH, Flinois JP, Beaune PH. Cytochrome P4502C9 is the principal catalyst of racemic acenocoumarol hydroxylation reactions in human liver microsomes. Drug Metabolism and Disposition,2000:28(11):1284–1290.
28. Trailokya A. Acenocoumarol in thromboembolic disorders. Cardiovascular Pharmacology,2015:4(4):1–4.
29. Ufer M. Comparative pharmacokinetics of vitamin K antagonists, warfarin, phenprocoumon and acenocoumarol. Clinical Pharmacokinetics,2005:44(12):1227–1246.

30. Verhoef TI, Redekop WK, Daly AK, Van Schie RM, De Boer A, Maitland-van der Zee AH. Pharmacogenetic-guided dosing of coumarin anticoagulants, algorithms for warfarin, acenocoumarol and phenprocoumon. British Journal of Clinical Pharmacology,2014:77(4):626–641.
31. Vu TT, Gooderham M. Adverse drug reactions and cutaneous manifestations associated with anticoagulation. Journal of Cutaneous Medicine and Surgery,2017:21(6):540–550.