

Vitamin K oral anticoagulant

Inhibition of the synthesis or activity of [Factor X](#) is the [mechanism of action](#) for many [anticoagulants](#). [Warfarin](#), a synthetic derivative of [coumarin](#), is the most widely used [oral anticoagulant](#) in the US. In some European countries, other coumarin derivatives ([phenprocoumon](#) and acenocoumarol) are used. These agents are [vitamin K antagonists](#) (VKA). Vitamin K is essential for the hepatic synthesis of Factors II (prothrombin), VII, IX and X.

Despite the application of many parenteral (unfractionated [heparin](#) and [Low-molecular-weight heparins](#)) and [oral anticoagulant vitamin K](#) antagonist (VKA) drugs, the prevention and treatment of venous and arterial [thrombosis](#) remain major medical challenges.

Vitamin K oral anticoagulant drugs are 4-hydroxycoumarin derivatives, which exert their anticoagulant effect by inhibiting vitamin K epoxide reductase and, possibly, vitamin KH2 reductase ¹⁾.

These compounds act by reducing vitamin KH2 (reduced form of vitamin K) levels, thereby limiting the cofactor effect of vitamin K on the γ -carboxylation of the vitamin K-dependent coagulation factors II, VII, IX, and X. VKAs also limit the effect of anticoagulant proteins, protein C and protein S, resulting in an inhibition of these proteins ^{2) 3)}.

During the last 60 years, [vitamin K](#) antagonists (VKAs), which include coumarin derivatives (eg, warfarin and acenocoumarol), have been the only [oral anticoagulants](#) used ⁴⁾.

The VKA dose is determined on an individual basis (not fixed), whereas novel [non vitamin K oral anticoagulant](#) are administered in fixed doses, except when a patient has a functional disorder of the liver or kidney.

The evolution of [vitamin K](#), from a dietary deficiency in birds to a postribosomal modifier of prothrombin in man, has been a fascinating scientific saga. Its antivitamin, the oral anticoagulant drugs, has been a powerful probe both of vitamin K action and of drug interactions. These agents have emerged from a limbo of clinical therapeutics to become a light of human pharmacology ⁵⁾.

Indications

Treatment with VKAs is indicated in various medical situations, such as for the treatment of Deep-Vein Thrombosis (Deep-vein thrombosis) and pulmonary embolism (PE), and the prevention of recurrence, atrial fibrillation (AF) and stroke in patients with NVAf, acute myocardial infarction, and vasculopathy, as well as in patients with tissue heart valves or mechanical prosthetic cardiac valves. These drugs are also used as prophylaxis for VTE in high-risk patients (eg, post-orthopedic surgery, embolic peripheral, and arterial disease) ^{6) 7)}.

Complications

[Intracranial haemorrhage](#) (ICH) is the most feared [complication](#) of [oral anticoagulation](#) for patients on [vitamin K antagonists](#) (VKAs).

This concerns mostly patients with [atrial fibrillation](#) or venous thromboembolism, or those carrying

mechanical heart valves. The incidence of VKA-associated ICH is 0.7% per year with atrial fibrillation⁸⁾ and 0.5% per year in the patients with a mechanical heart valve⁹⁾.

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