

Clover, Rats & Geopolitics: Episodes in warfarin's history

Origin Story



For rural farmers in the US, the great depression started in the 1920s. Exports to Europe ceased and the price of wheat fell. In addition, American and Canadian cattle were mysteriously dying from what Frank Schofield identified as Sweet Clover Disease. Hay, containing sweet clovers (*Melilotus alba* and *Melilotus officinalis*) were rotting, due to a series of wet summers, and the moulds *Penicillium nigricans* and *Penicillium jensi*. These were oxidising coumarin - the chemical responsible for the smell of newly mown hay - into dicoumarol, and this was causing internal bleeding in the cattle, leading to death.



Warfarin is one of the most commonly prescribed drugs in the world. Its anticoagulant action has saved millions of lives and it continues to be the anticoagulant of choice. Warfarin's history all started in the US and Canada during the 1920s.

Here's how the story goes: Ed Carlson a local farmer had lost many of his herd to the Sweet Clover Disease. In desperation, he drove through a blizzard, to the Wisconsin Alumni Research Foundation, with a can of un-coagulated blood, a pile of rotting hay and a dead half frozen cow. He presented these to Karl Link and his senior research student, Wilhelm Schoeffel. They started to investigate the Sweet Clover Disease and isolated the active compound, dicoumarol. They then developed an analogue of dicoumarol, which has a strong anticoagulation action - coumadin. This was named after the Wisconsin Alumni Research Foundation, where the work was performed - warfarin.

Rat Poison



Karl Link marketed dicoumarol as a rat poison in 1948. Within about 10 years, rats started to become resistant to the chemical. Humans can also develop warfarin resistance, particularly after anticoagulant therapy.

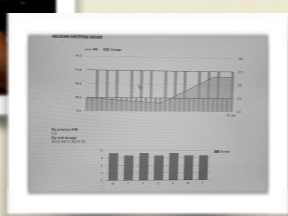
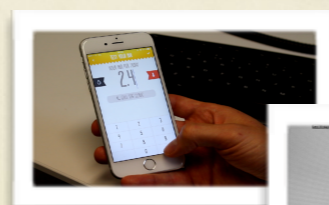
Cold War Leaders

The American President Dwight D. Eisenhower (right) was prescribed warfarin after suffering a heart attack, and this popularised the new medical use of warfarin.



One of the enduring conspiracy theories of the mid 20th century is that Joseph Stalin, dictator of the Soviet Union was poisoned. The official cause of his death was a stroke. However, Stalin's unusual symptoms - bleeding stomach, vomiting blood and bleeding in the heart could have been the result of warfarin poisoning. Warfarin, which is clear, crystalline and tasteless could have been administered to his wine the night before by one of his inner circle. An average adult fatal dose is about 15mg.

Digital Warfarin



Warfarin requires careful management to enable patients to get the best outcomes. For this reason, it is now in the forefront of 'going digital.' Research, distribution, supply, prescribing and monitoring are now achieved electronically.