

PHARMACY *a long and proud history*

BLOOD AND ANTICOAGULANTS

In 1922 cattle in North Dakota were found bleeding to death from minor injuries, or dropping dead from internal bleeding with no sign of injury.

Francis Schofield a veterinary pathologist found that the bleeding was caused by the cattle eating mouldy hay (silage) made from sweet clovers, which had been introduced from Europe earlier in the century because they could withstand the harsh winters and dry summers of North Dakota. This silage acted as a powerful anticoagulant, prolonging the cattle's blood clotting time causing internal bleeding and death.

In 1929 Dr Lee Roderick found that cattle with **sweet clover disease** had great deficiencies of **prothrombin** a protein necessary for blood clotting.

Meanwhile a Danish chemist Carl Dam had discovered that an 'unknown factor' was necessary for blood coagulation and in 1935 he named it **vitamin K**.

It was proved that vitamin K is necessary for the formation of prothrombin, which is a precursor to the clotting agent **thrombin**. However, the identity of the anticoagulant in the silage remained a mystery until 1940 when Karl Link and his colleagues identified it as a **coumarin** derivative that was eventually patented in 1941 as **dicumarol** and marketed as an effective anticoagulant to treat thrombosis.

Link continued his research, seeking more powerful anticoagulants and synthesized over a 100 variants of dicumarol. In the process he found derivatives that were great rat killers (they died from internal bleeding). In 1948 the most effective derivative was registered as **warfarin**, so named after the **Wisconsin Alumni Research Foundation** that was supporting his research plus **arin** from **coumarin**. Two years later, when dicumarol was facing competition from European medicines, Link tried with no success to convince doctors to use warfarin on humans.

Then in 1951 a naval recruit tried to commit suicide (unsuccessfully) by taking 567 mg of warfarin rat killer. The doctors then agreed that warfarin would be safe for human use and was more effective than dicumarol.

It was not until 1978 that scientists discovered exactly how warfarin worked.

In pharmaceutical terms warfarin inhibits the enzyme vitamin K – epoxide reductase – thereby blocking the action of Vitamin K and preventing blood clotting.

In every-day language warfarin works by preventing the vitamin K-dependent production of clotting factors.

BLOOD CLOTTING BRIEFLY

Blood cells called platelets clump together at an affected site and produce chemicals (proteins made in the liver) that activate clotting factors in the blood. These clotting factors (which depend on vitamin K to work) convert a protein called Fibrin into Fibrinogen and the Fibrinogen binds the platelets together forming a blood clot.

*What an incredible machine our body is.
It even repairs itself.*