

The Factor in Dicumarol Plasma Which Accelerates the Coagulation of Plasma from Vitamin K-Deficient Chicks

ØYVIND SØRBYE*, INGER KRUSE and HENRIK DAM

Department of Biology, Polytechnic Institute, Copenhagen, Denmark

Recently¹ we reported the concentration of a protein factor in plasma from vitamin K-deficient chicks accelerating the coagulation of plasma from dicumarolized chicks. This factor — tentatively called the κ -factor — is essential for the understanding of the "anomalous" prothrombin times obtained for mixtures of plasmas from vitamin K-deficient and from dicumarol-poisoned chicks — as described by Dam and Søndergaard². In dicumarol plasma the concentrations of prothrombin and κ -factor are reduced; only after addition of optimal amounts of κ -factor will a dicumarol plasma be a purely hypoprothrombinemic plasma. Prothrombin times of mixtures of plasma from dicumarolized and from vitamin K-deficient chicks also indicated that there is an agent in dicumarol plasma capable of accelerating the coagulation of vitamin K-deficient plasma.

It has now been possible to concentrate this agent — a protein factor — from plasma of severely dicumarolized chicks (prothrombin time 20 to 25 times the normal value) by means of adsorption and elution procedures. It shows the following properties:

1. It is completely adsorbed from plasma of dicumarolized chicks by treatment of the plasma with 1 % by weight of BaCO₃. It can be eluted from the adsorbent by a solution of sodium citrate.

* Fellow 1950—51: Norwegian Research Council for Technical and Natural Sciences.

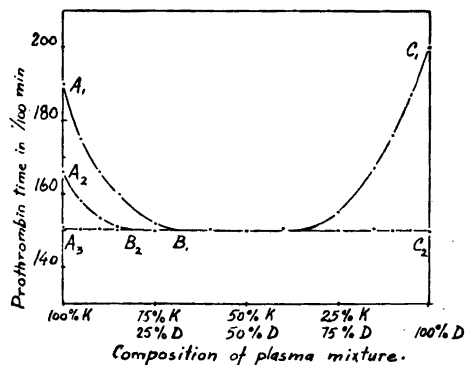


Fig. 1. Prothrombin time as a function of the composition of plasma mixtures.

K: plasma from a vitamin K-deficient chick.
D: plasma from a dicumarol poisoned chick.

2. Addition of small amounts of the protein to dicumarol chicken plasma has no influence on the prothrombin time.

3. It has no influence on the prothrombin time of fresh normal chicken plasma nor on the prothrombin time of stored chicken plasma.

4. Addition of small quantities of the protein to vitamin K-deficient chicken plasma reduces the prothrombin time to a certain extent. Addition of greater amounts has no further influence on the prothrombin time.

Highly active preparations of factor V (from chicken plasma) had no accelerating effect on the prothrombin time of the vitamin K-deficient plasma used in these investigations.

A typical form of the curve representing the prothrombin time for mixtures of a dicumarol and a vitamin K-deficient plasma as a function of the composition of the plasma mixture is shown in Fig. 1 (curve A₁-B₁-C₁). The result of the addition of a constant extremely small amount of the new coagulation protein to all mixtures is shown by the curve A₂-B₂-C₁.

The effect of optimal amounts of the protein added to all plasma mixtures is represented by the curve A₃-B₂-C₁.

We have called the new factor the δ -factor. This is meant to be a preliminary name until enough evidence concerning its exact function in prothrombin activation has accumulated to make a rational and systematic name possible.

The δ -factor is distinctly different from prothrombin, factor V and the κ -factor.

The effect of optimal amounts of the κ -factor on the prothrombin time of mixtures of a vitamin K-deficient and a dicumarolized plasma is represented by the curve A₁-B₁-C₁.

When optimal amounts of both the δ - and the κ -factors are added to all plasma mixtures, the curve is straightened out to give the line A₂-B₂-C₂. This is the type of curve that would be expected to represent the prothrombin time of mixtures of two purely hypoprothrombinemic plasmas having identical prothrombin content.

The deficit in δ -factor arises when chicks are fed on an artificial diet deprived of vitamin K. So far there are no indications that the δ -deficiency is caused by lack of another dietary factor than vitamin K. On the other hand, dicumarol — known as a potent inhibitor of the prothrombinogenic effect of vitamin K — does not seem to cause any significant reduction of the amount of the δ -factor in chicken plasma, at least not below the optimal level.

The properties and functions of the δ - and the κ -factors are being studied further.

1. Serbye, Ø., Kruse, I., and Dam, H. *Acta Chem. Scand.* 4 (1950) 549.
2. Dam, H., and Søndergaard, E. *Biochem. et Biophys. Acta* 2 (1948) 409.

Received June 24, 1950.

