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Short Communication

The Factor in Vitamin K-Deficient Plasma which Accelerates the Coagulation of Dicumarol Plasma

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Several published studies [1–4] support the assumption that the coagulation anomaly produced by the administration of dicumarol is not a mere hypoprothrombinemia.

In experiments with chicken plasma Dam and Søndergaard [4] observed that small amounts of vitamin K-deficient plasma added to dicumarol plasma shortened the prothrombin time of the latter and vice versa. They explained this effect by assuming that the two plasmas are primarily lacking one and the same component (prothrombin) whereas in addition to this vitamin K-deficient plasma is lacking in another component and dicumarol plasma in a third.

By means of adsorption and elution procedures we have now isolated a small protein fraction from plasma of vitamin K-deficient chicks. This fraction contains the agent which shortens the prothrombin time of dicumarol plasma.

The protein thus isolated shows the following properties:

1. It is completely adsorbed from oxalated plasma of vitamin K-deficient chicks when the plasma is treated with one per cent of its weight of barium carbonate. It can be eluted from the adsorbent with citrate.

2. Addition of small amounts of this protein to dicumarol chicken plasma reduces the prothrombin time of the latter to a certain extent; the addition of larger amounts of the protein causes no further reduction of the prothrombin time.

3. Addition of the protein to plasma from vitamin K-deficient chicks does not alter the prothrombin time.

4. The protein has no effect on the prothrombin time of stored chicken plasma.

5. When stored chicken plasma is supplied with small amounts of the most labile factor of chicken plasma (corresponding to factor V in mammals), the addition of the new factor shortens the prothrombin time further.

In the dicumarol plasmas used in the present investigations the amount of the most labile factor is not reduced below its optimal concentration.

Fig. 1 shows how the curve (A–B) – representing the prothrombin time of mixtures of a dicumarol plasma with a vitamin K-deficient plasma – is straightened out (A–C) by the addition of a constant amount of the new factor so that the curvature otherwise occuring at the high concentrations of dicumarol plasma is eliminated.

Even when the preparation contains some prothrombin, the curve is straightened out in the same way (A′–C′), in this case shifted to somewhat lower prothrombin times, compared with the curve (A–C) resulting from a mere addition of the new factor.

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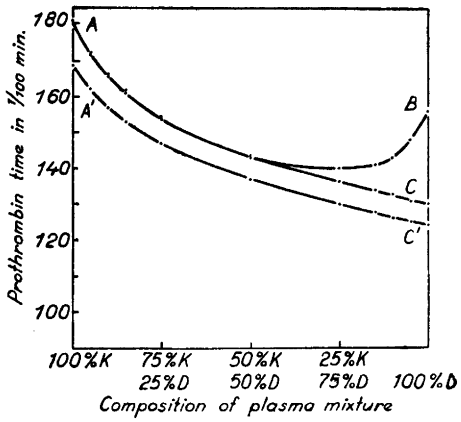

Fig. 1. Prothrombin time as a function of composition of plasma mixture.
K: plasma from vitamin K-deficient chick.
D: » » dicumarol-poisoned »

We have called this new factor the *x*-factor in absence of an appropriate name characterizing its function in prothrombin activation. Its adsorption characteristics are very similar to those of prothrombin, but it is distinctly different from this protein. It is also different from the most labile factor in chicken plasma (corresponding to factor V of mammalian plasma). It seems possible that the *x*-factor of chicken plasma could have the same function as the factor in mammalian plasma, which on coagulation gives rise to the SPCA (serum prothrombin conversion accelerator) of Alexander and co-workers [5]. The synthesis of the *x*-factor is obviously independent of vitamin K.

The properties and function of the *x*-factor are being studied further.

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2. Owen, C. A., and Bollmann, J. L. *Proc. Soc. Exp. Biol. Med.* **67** (1948) 231.
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4. Dam, H., and Søndergaard, E. *Biochim. Biophys. Acta* **2** (1948) 409.
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Dihydroxyphenylalanine and Hydroxytyramine in Mammalian Suprarenals

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In addition to adrenaline, extracts of mammalian suprarenals have recently been shown to contain *nor*adrenaline (Holtz and Schümann [1], Goldenberg, Faber, Alston and Chargaff [2], Bergström, Euler and Hamberg [3]). Hitherto, there has been no indication in the suprarenals of other catechols (Goldenberg *et al.*[2]). However, it is said that hydroxytyramine occurs in urine (Holtz) and has recently been found in extracts of heart (Goodall)[4].

When the suprarenal extracts of sheep were subjected to paper chromatography, an additional catechol spot was observed. This spot was identical with hydroxytyramine both as to color and to position. Further, this identity was substantiated by exposing the extract chromatogram to two different solvent systems, *i. e. N*-butanol/*N*HCl and phenol/H_2O.

In the suprarenal extracts prepared from thyroidectomized sheep, another spot has been observed. This spot, however, agreed in position and color with dihydroxyphenylalanine (DOPA). Again the identity was substantiated by preparing the paper chromatogram with different effluents, butanol and phenol.

The presence of hydroxytyramine in normal sheep suprarenals and of DOPA in the suprarenals of thyroidectomized sheep is suggestive of the role that hydroxytyramine and DOPA may play as precursors to *nor*adrenaline, and also the possible importance of thyroxin to such a change. Blaschko [5] first suggested these compounds as precursors to *nor*adrenaline.

1. Holtz, P., and Schümann, H. J. *Naturwissenschaften* **35** (1948) 159.