A TISSUE ENZYME RESEMBLING STEWART – PROWER X FACTOR

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Extracts of skeletal and heart muscles, kidneys, liver, and brain of dead persons significantly shorten the prothrombin time of plasma not containing Stewart–Prower factor; extracts of lung parenchyma are an exception to this rule. Plasma X factor is utilized intensively during blood clotting.

Recent work has shown that the tissues play an active part in local hemostasis and in the regulation of blood clotting [1-6]. In particular, the writers have shown that the tissues contain thromboplastic and fibrinolytic substances, enzymes resembling the plasma V, VII, and XIII factors, inhibitors of fibrinolysis, natural anticoagulants, activators of plasma factors V and VII, and substances inducing aggregation and viscous metamorphosis of platelets. The presence of a group of active hemocoagulating compounds in the tissues has led to the development of the concept of a tissue blood clotting system, functioning concurrently with the humoral hemocoagulatory system [2-6]. An enzyme with the properties of Stewart–Prower X factor was discovered by the writers in the placenta and decidual membrane. It was therefore decided to investigate whether a similar enzyme exists in other tissues. The results of this investigation are described below.

EXPERIMENTAL METHOD AND RESULTS

Extracts of the tissues of 14 cadavers of persons dying accidentally were studied. The skeletal and cardiac muscles, kidneys, liver, brain, lungs, and myometrium of nonpregnant women were investigated. Pieces of tissue were thoroughly washed to remove blood, dried with filter paper to an "air-dry" state, weighed, homogenized in 10 volumes of physiological saline, and centrifuged at 1500 rpm for 5 min. The properties of the supernatant were studied. Its effect on the prothrombin time was determined by the test using plasma without X factor, obtained by the method of Malhotra and Carter [8].

The extracts of most tissues studied significantly shortened the prothrombin time of plasma deficient in X factor (Table 1). Extracts of the lung parenchyma appreciably prolonged the prothrombin time of plasma with a low content of Stewart–Prower factor, due to the presence of large quantities of natural anticoagulants of heparin type in the lungs. The facts described indicate that many human tissues contain an enzyme similar to plasma X factor. This compound does not restore the normal prothrombin time of a test plasma deficient in Stewart–Prower factor, but it can partially replace this plasma enzyme in the activation of tissue, erythrocytic, and plasma thromboplastin, and also in the conversion of prothrombin into thrombin.

A substance activating X factor in the presence of phospholipids has been isolated from the rabbit brain [9]. Similar tests were carried out with all the tissues under investigation, but no activation of Stewart–Prower factor under the influence of the tissue extracts could be demonstrated, possibly on account of the insufficient sensitivity of the methods of determination.

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TABLE 1. Effect of Tissue Extracts on Prothrombin Time (in sec) of Plasma Deficient in X Factor (M ± m)

Tissue studied	No. of experiments	Control	Expt.
Skeletal muscles	12	201	161±3,9
Brain	9	201,5	162±8
Kidney	11	206,2	169,3±9,1
Heart muscle	13	197,3	163±11,4
Liver	13	197,5	172,2±4,1
Myometrium	4	185,5	152,2
Lungs	13	197,1	226,1±6,7

Note. $P < 0.001$.

The character of the role of X factor in blood coagulation has not yet been finally settled. In one view [7], it is a stable compound and is not utilized during formation of the blood clot. In another view [10, 11], Stewart–Prower factor is labile on keeping and is utilized in the first and second phases of hemocoagulation. To verify these hypotheses, the activity of X factor in the plasma and serum was studied 30, 60, 120, and 180 min after the formation of a blood clot and its incubation in a water bath at 37° for these times. These experiments showed that the activity of Stewart–Prower factor falls sharply during and after blood clotting, and the factor is utilized to a much greater extent than V factor.

For example, 30 min after the formation of a blood clot activity of Stewart–Prower factor in the serum formed by retraction and fibrinolysis was 66.7 ± 3.6%, after 120 min it was 44.3 ± 3.4%, and after 180 min 40.7 ± 1.8% of its activity in the plasma. These findings are in agreement with those of Niemetz [10, 11] and they confirm that X factor is utilized intensively during blood clotting.

The results of these experiments thus suggest that the components of the tissue blood clotting system include an enzyme similar to the Stewart–Prower plasma factor.

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