FIBRINOLYTIC ACTIVITY OF RAT TISSUE

Yu. P. Nikitin and T. A. Tabarovskaya

UDC 612.115.1-064-019:599.323.4

Experiments on rats (by the method of fibrinolysis macroautography) have shown that the lungs and kidneys contain the greatest amount of plasminogen activator. Definite fibrinolytic activity is also manifested by the adventitia of the aorta and the intima of the vena cava and pulmonary artery. The intima of the aorta has a lower content of plasminogen activator. Liver and spleen tissue is inactive. The presence of fibrinolysis inhibitors in the liver and in the media of the aorta has been demonstrated.

* * *

Very little is known of the fibrinolytic properties of organs and tissues of albino rats. Permin [6], Albrechtsen [2], and Warren [9] give brief details of the fibrinolytic activity of some organs of these animals. These workers used methods giving information about plasminogen inhibitor only or the total fibrinolytic effect without distinction between the separate components of the fibrinolytic system.

The objects of the present investigation were, first, to determine the fibrinolytic activity of the most important internal organs and tissues of healthy rats, and second, to make a separate study of their plasmin and plasminogen activator and proactivator content.

EXPERIMENTAL METHOD

The method of fibrinolysis macroautography, based on the fibrin film technique [3], was used. This semiquantitative method can be used to determine the content of fibrinolytically active substances in the tissues. Thin pieces of equal shape and size were excised from the test tissue washed free from blood with cold physiological saline. Vessels and tissue membranes were placed on chemically pure filter paper and cut together with it into squares about 9 mm^2 in area. The samples were placed on films of unheated bovine fibrin. Lysis of these films can take place through the intervention of plasmin and (or) plasminogen activator (bovine fibrin always contains plasminogen as an impurity). To detect plasmin alone, fibrin freed from plasminogen by heating to 85° for 45 min was used [5]. To detect plasminogen proactivator, 100-1000 units streptokinase was added to the fibrinogen solution before clotting. The results were read after incubation for 18 h at 37°. The size of the zones of fibrinolysis was expressed conventionally in points. Partial lysis beneath the tissue sample (not completely through the film) was denoted as ±, complete lysis of fibrin beneath the sample and around it for 2-3 mm was denoted by 1 point (+), larger areas of lysis by 2 and 3 points (++ and +++), and absence of lysis by (−).

EXPERIMENTAL RESULTS

The highest fibrinolytic activity was found in the lung tissue of the rats (Table 1). Its content of plasminogen activator was very high, and that of plasmin low. In the kidney, the medulla showed high activity. In the capsule of the kidney comparatively little of the substances activating fibrinolysis were present, while in human kidney the highest content of plasminogen activator is found in the capsule [4].

A definite fibrinolytic effect was given by the serous membrane and fascia of the skeletal muscles. They contained no plasmin, but plasminogen activator was consistently discovered.

In the aorta, the adventitia possessed marked fibrinolytic activity. The media did not contain plasminogen activator but, conversely, substances inhibiting fibrinolysis were found in it. These were demonstrated by the absence of fibrinolytic action of the adventitia if preliminarily ground in a mortar with a small quantity of media from the same aorta. A sample of aorta consisting of adventitia and adjacent parts of the media, if placed on a fibrin film beneath tissue of the media, exhibited lower fibrinolytic activity than

Novokuznetsk Postgraduate Medical Institute. (Presented by Academician V. V. Parin.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 67, No. 6, pp. 19-21, June, 1969. Original article submitted May 20, 1967.

TABLE 1. Fibrinolytic Activity of Rat Tissues

Tissue investigated	No. of cases	Heated fibrin	Unheated fibrin	Fibrin with streptokinase
Lung	17	±	+++	+++
Kidney				
Medulla	15	–	++	++
Cortex	15	–	+	+
Kidney capsule	4	–	+	+
Fascia of muscles	12	–	+	+
Pleura	9	–	+	+
Pericardium	9	–	+	+
Peritoneum	10	–	±	±
Vena cava				
Intima	18	–	+	+
Adventitia	17	–	+	+
Pulmonary artery				
Intima	14	±	+	+
Adventitia	12	±	+	+
Aorta				
Intima	33	–	±	±
Media	5	–	–	–
Adventitia	26	–	+	+
Brain			+	+
Gray matter	9	–	+	+
White matter	8	–	+	+
Lymph gland	8	–	+	+
Adrenal	7	–	+	+
Myocardium	17	–	+	+
Skeletal muscle	17	–	±	±
Liver	12	–	–	–
Spleen	10	–	–	–
Whole blood	20	–	–	–
Blood plasma	20	–	–	–
Euglobulins of blood plasma	20	±	+	+

if applied on the fibrin beneath adventitia. This also indicated that the media of the aorta contains agents inhibiting fibrinolysis. The inner (endothelial) surface of the aorta exhibited fibrinolytic activity, but weaker than the adventitia. This difference may be due to the fact that the intima of the rat aorta is technically difficult to separate from the media, so that the sample of intima usually included tissue from the media which could have inhibited fibrinolysis.

The content of plasminogen activators was higher in the wall of the inferior vena cava and, in particular, of the pulmonary artery than in the aorta, and in these two vessels, moreover, not only the adventitia but also the intima exhibited high activity. In contrast to the aorta, in whose wall plasmin was very rarely detected (and even if it was, it was present only in negligible traces), the wall of the pulmonary artery contained active fibrinolytic enzyme more frequently and in somewhat higher quantities.

Plasminogen activator was found in the brain, lymph gland, and adrenal tissues, and in smaller amounts in the myocardium and skeletal muscle. It was not found in liver or spleen tissue.

Streptokinase had no appreciable effect on the fibrinolytic activity of the rat tissues. Samples of these tissues formed identical zones of lysis of unheated fibrin both in the absence or the presence of streptokinase in fibrin films (Table 1).

The difference between the fibrinolytic activity of different rat organs may be due to differences in the concentration of plasminogen activator. This is the usual explanation given of results of analogous investigations of the tissues of other animals and man [1, 7, 8]. However, another investigation is possible.

The contents not of activating substances, but of inhibitors of fibrinolysis may differ in different tissues. If a liver homogenate is prepared and mixed with homogenate of lung tissue, the latter loses its high fibrinolytic activity. Consequently, the rat liver contains large amounts of antifibrinolytic substances capable of blocking the action of plasminogen activator. The difference between the fibrinolytic activity of different organs and tissues may perhaps be due to differences in the content of fibrinolysis inhibitors, and not only to differences in the level of plasminogen activator which, indeed, may play a subordinate role.

LITERATURE CITED

1. O. K. Albrechtsen, Brit. J. Haemat., 3, 284 (1957).
2. O. K. Albrechtsen, Acta Physiol. Scand., 47, Suppl. 165 (1959).
3. T. Astrup and S. Mülertz, Arch. Biochem., 40, 346 (1952).
4. T. Astrup, in: Proceedings of the 6th International Congress of Gerontology, Copenhagen (1964), p. 356.
5. M. Lassen, Acta Physiol. Scand., 27, 371 (1952).
6. P. M. Permin, Acta Physiol. Scand., 21, 159 (1950).
7. H. Sandberg, M. Rezai, T. T. Bangayan, et al., J. Lab. Clin. Med., 61, 592 (1963).
8. H. Stamm, Geburtsh. und Frauenheilk., 24, 1034 (1964).
9. B. A. Warren, Brit. J. Exp. Path., 44, 365 (1963).