THE EFFECT OF SUBSTANCES STIMULATING AND DEPRESSING
THE CENTRAL NERVOUS SYSTEM ON THE QUANTITY
AND QUALITY OF CORTICOSTEROIDS IN THE BLOOD
OF DOGS AND GUINEA PIGS

N. P. Goncharov

Department of Pharmacology (Head - AMN SSSR Active Member Prof.
S. V. Anichkov) of the Leningrad Medical Institute of Sanitary Hygiene
(Presented by AMN SSSR Active Member S. V. Anichkov)
Translated from Byulleten' Eksperimental'noi Biologii i Meditsiny,
Vol. 52, No. 11, pp. 76-79, November, 1961
Original article submitted February 27, 1961

This work was carried out to study the effect of the neurotropic substances Dibazol and Diphenin on the hypo-
physis - adrenal cortex system.

Dibazol stimulates the central nervous system [1]. Diphenin, on the other hand, depresses certain centers of
the brain (anticonvulsive, inhibits calomel secretion, decreases the amount of gastric juice during the reflex phase
of secretion) [4, 8].

EXPERIMENTAL METHODS

We studied the effect of these substances on the adrenocortical function of male dogs weighing 20-25 kg each.

Our first undertaking was to determine the effect of Dibazol and Diphenin on the concentration of 17-hydroxy-
corticosteroids in the plasma of peripheral blood taken from the lateral vein of the dog's leg. The Silver and Porter
method as modified by N. A. Yudaev and Yu. A. Pankov [10] was used to determine the content of 17-hydroxycor-
ticosteroids. The low level of 17-hydroxycorticosteroids in these dogs (less than 0.5 γ% in two dogs and 1γ% in one)
made it impossible to determine any authentic pattern of change in the 17-hydroxycorticosteroid content of the peri-
pheral blood plasma.

We used the following method in order to obtain blood with a higher content of 17-hydroxycorticosteroids in
the plasma: the dog was put under ether-oxygen endotracheal anesthesia, and an incision was made along the middle
line of the abdomen. The section of the caudal vena cava with the renal and lumboadrenal veins was dissected out.
Through an incision in the femoral vein, a polyethylene catheter was inserted somewhat cranial to the mouths of the
lumboadrenal veins. When the catheter inserted was ascertained to have reached the required level, the vena cava
was ligated caudal to the renal veins.

This method permits determination of 17-hydroxycorticosteroids in higher concentrations than are found in the
peripheral blood.

At the mouths of the lumboadrenal veins, the 17-hydroxycorticosteroid content was four times that in the peri-
pheral blood. The catheter was filled with heparin when no blood was being taken. Three to four days after the
operation, when the increased 17-hydroxycorticosteroid content induced by the operation had returned to the normal
level, we began taking blood samples from the mouths of the lumboadrenal veins.

We first determined the control level of the 17-hydroxycorticosteroid content in the dogs. Over a period of
30-50 days, 20 ml of blood for two parallel determinations was taken 5-6 times from each dog at intervals of 1-2
days. We next determined the 17-hydroxycorticosteroid content under the influence of Dibazol or Diphenin, the
latter being introduced into the polyethylene catheter in a dose of 20 mg/kg each. Blood samples were taken 90 min
after the administration of the experimental substance. The 17-hydroxycorticosteroids were determined by the meth-
od mentioned above.
As the figure shows, the 17-hydroxycorticosteroid content of the blood plasma doubled under the influence of Diphenin and increased 2 1/2 times under that of Dibazol. Statistical processing of the experimental results proved the effect observed to be significant.

The results obtained are in accord with the literature data [3, 7, 5, 6, 2, 9], which indicate that Dibazol raises the resistance of the organism to different harmful influences, and this effect could easily be the result of a stimulating influence on the hypophyseal–adrenal system.

Diphenin possesses an antidiuretic effect [4] associated with its influence on the secretion of the antidiuretic hormone. It has been established on the basis of much experimental data [12, 13, 14, 15] that ACTH secretion is stimulated by the antidiuretic hormone or by a substance with a polypeptide structure very similar to the latter. One can therefore propose that the antidiuretic hormone participates in the activation of adenohypophysial production of ACTH effected by Diphenin. It has been established that the intravenous injection of 7-10 units of exogenous ACTH induces the same effect.

The regular increase of the 17-hydroxycorticosteroid content in the plasma of the dogs' caudal vena cava being apparent, qualitative determination of the corticosteroids in the peripheral blood plasma following the action of the experimental substances was our next undertaking.

These experiments were performed on 20 male guinea pigs weighing 600-800 g each. Ten of the guinea pigs were injected intraperitoneally with Dibazol (30 mg/kg) or Diphenin (20 mg/kg) prepared in an alkaline solution. The other ten guinea pigs were intraperitoneally injected with distilled water (control for experiments with Dibazol) or an alkaline solution (control for experiments with Diphenin). The alkalinity of the control solution was the same as that of the Diphenin solution. Two hours after the dibazol or Diphenin injection, 8-10 ml of blood was taken from the cardiac cavity of each guinea pig. So that the animals would not die, we put them in a head-down position for 1-2 min immediately after the blood was taken and administered 8-10 ml of a physiological solution intraperitoneally.

Effect of Dibazol and Diphenin on the concentration of 17-hydroxycorticosteroids in the plasma of blood from the caudal vena cava of a dog. 1) Control; 2) Dibazol; 3) Diphenin. Vertical line – significant range of mean.