Effect of Reserpine on the Nucleotide and Catecholamine Content of the Denervated Adrenal Medulla of the Rat

Reserpine causes a depletion of the catecholamines and adenosine triphosphate stored in the amine granules of the adrenal medulla[1–3]. This effect may, however, have been produced indirectly through the secretory nerves[3]. Such a stimulation of the medulla induced by insulin hypoglycæmia or morphine causes a concomitant release of amines and adenosine triphosphate[4,5]. The essential problem, however, is how reserpine causes amine depletion by direct action on the cells. As a preliminary attempt to elucidate this problem, the effect of reserpine on the nucleotide and amine content of the denervated rat medulla was studied.

The left adrenal medulla of twelve male rats (body-weight 350–400 gm.) was denervated by cutting the splanchnic nerves. This produces a total denervation[7]. After ten days the animals were divided into three equal groups. Reserpine (10 mgm./kgm. subcutaneously) was administered to each of the rats. The animals were killed 24 hr. after the injection and the adrenal medullæ were dissected, extracted and analysed for catecholamines and adenosine phosphates by means of high-voltage paper electrophoresis in the way described in a previous paper[6]. This method yields values for the adenosine phosphates which are somewhat higher than the real ones owing to the presence of other nucleotides[3]. Each extract contained the four left or right medullæ from the rats in each group. The rats were of the same weight and stock as those used in an experiment made at the same time. The normal animals in that work[6] were therefore taken as controls. Denervation of the medulla does not produce any certain changes of the nucleotide or amine content[6].

The results are presented in Table 1.

Table 1. μMOLES IN MEDULLÆ FROM 4 GLANDS

		Catechol-amines	ATP	ADP	AMP
Normal glands	Mean	0·365	0·0845	0·0315	0·0096
Reserpine Denervated glands	I	0·280	0·0650	0·0235	0·0077
	II	0·190	0·0415	0·0225	0·0061
	III	0·230	0·0550	0·0215	0·0070
	Mean	0·235	0·0540	0·0225	0·0069
		−36%	−36%	−29%	−28%
Non-denervated glands	I	0·110	0·0245	0·0175	0·0063
	II	0·0570	0·0140	0·0115	0·0048
	III	0·0915	0·0200	0·0130	0·0052
	Mean	0·0860	0·0195	0·0140	0·0054
		−76%	−77%	−56%	−44%

Reserpine produced an amine depletion which was on an average 77 per cent in the normal glands and 36 per cent in the denervated ones. As previously found for normal medulla in fowl[1], rat[2], and sheep[3], disappearance of a corresponding amount of adenosine triphosphate occurred in both the normal and the denervated glands. The adenosine monophosphate and adenosine diphosphate content also decreased, but to a lesser extent.

Thus it seems that the release of amines from the adenosine triphosphate amine storage complex produced by reserpine through direct action on the cells is accompanied by a release and/or breakdown of an equivalent amount of adenosine triphosphate which, furthermore, does not lead to an accumulation of adenosine diphosphate or adenosine monophosphate. In this respect the direct reserpine action and the action of nervous secretory stimuli give a similar effect. This may mean that both reserpine and secretory stimuli act through the same mechanism (for example, activation of a release or inhibition of a storage mechanism). Considering the structure of the adenosine triphosphate amine storage complex[8], it seems probable, however, that an amine release—irrespective of the way in which it is brought about—must always be accompanied by a corresponding release (or breakdown) of adenosine triphosphate. The findings, therefore, only seem to imply that the amines released from the granules by reserpine do not accumulate to any appreciable extent in the cytoplasmic sap.

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Effect of Three Compounds related to Diethylstilbœstrol on the Phagocytic Activity of the Reticulo-Endothelial System

It has been reported previously that diethylstilbœstrol is a strong stimulant of the phagocytic activity of the reticulo-endothelial system[1]; that the minimum dose required to stimulate the phagocytes is about 100 times greater than that necessary to induce œstrus[2]; and that after treatment with 0·5 mgm. diethylstilbœstrol daily for six days the phagocytic activity returns to within normal control limits in about eight days[3].

The present communication is a report of the action on the phagocytic activity of the reticulo-endothelial system of three compounds related to diethylstilbœstrol.

Twenty-five male white mice (*T.O.* Swiss strain) of 20–25 gm. body-weight were used in these experiments. Five animals were used to test each compound, each animal receiving one subcutaneous dose of 0·5 mgm. of the compound in 0·05 ml. arachis oil daily for six days. On the eighth day after the commencement of the treatment the phagocytic activity was measured by the rate of disappearance of a known amount of specially prepared carbon from the circulating blood[4], the procedure used being that described in previous communications[1], and the total-body phagocytic activity or phagocytic index being denoted by the symbol *K*.

Ten of the animals were used as controls and were given 0·05 ml. arachis oil once daily for six days. The phagocytic activity was then measured on the eighth day by the carbon method referred to above. The arachis oil controls showed a phagocytic index or *K* value of $13 \pm 2{\cdot}4$.

The results are shown in Table 1. The three compounds are active œstrogens, and it can be seen that all of them are strong stimulants of phagocytic activity. These results again suggest that the configuration of the molecule which confers œstrogenic activity is also essential for reticulo-endothelial stimulation. In addition, the results show that phagocytic stimulation