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Certain Factors in the Preparation of Cortin.*

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The potency of the extracts used in this study has been tested by the effect on the growth of young adrenalectomized white rats.[1] This test has been carried out immediately after adrenalectomy as that is the most crucial period of adrenal insufficiency. Sometimes when the animals have failed to grow they have been further tested by their resistance to cold,[2] comparison being made with adrenalectomized rats treated with adequate cortin.

In an earlier work on the hormone of the adrenal cortex in which it was salted out with the globulins[3] we found that exposure of the precipitate to air for a few hours reduced the potency. Moreover heating the extract of the sodium chloride precipitate to 80°C. for 5 min. with stirring, to cause admixture with air, destroyed the hormone.[4] From this evidence we concluded that it was necessary to operate in the absence of O_2. Distillation of the ether at atmospheric pressure in the preparation by the ether-alcohol method[4] produces a less potent extract than when the distillation is *in vacuo*. Heating the concentrated extract in an open beaker for one hour at 80°C. without stirring does not appreciably destroy the hormone. The extract can be boiled for a short period (5 minutes) in the absence of oxygen without great loss of potency.

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1 Hartman and Thorn, PROC. SOC. EXP. BIOL. AND MED., 1930, **28**, 94.

2 Hartman, PROC. SOC. EXP. BIOL. AND MED., 1931, **28**, 702.

3 Hartman, Brownell, Hartman, Dean and McArthur, *Am. J. Physiol.*, 1928, **86**, 353.

4 Hartman, Brownell and Hartman, *Am. J. Physiol.*, 1930, **95**, 670.

Small amounts of antioxidants, such as hydroquinone, resorcinol or levulose retard the loss of potency in aqueous solution. The hormone can be preserved in 80-95% alcohol for weeks. Cortin is very unstable in the presence of the fixed alkalies. It seems to be completely destroyed by tenth normal NaOH at 20°C. in less than one hour. On the other hand tenth normal NH_4OH under the same conditions has little or no effect. Tenth normal HCl at 20°C. for one hour is without effect. Extraction of the dry residue with water for the final product must not be aided by heat nor must it proceed for a long period because toxic substances are absorbed. An extract made by allowing water to stand on the residue for one hour at 45°C. when injected into adrenalectomized animals caused inflammation and loss of weight.

We have made extracts of whole adrenals by many different methods in an attempt to separate cortin from the toxic substances which develop in the medulla.[5] No method has been found which yields as potent an extract per unit of cortex as does the simple method described. Active charcoal seems to remove both cortin and toxic substances from an aqueous solution (pH 8-6.5). Attempts to elute the hormone have been partially successful. Permutit removes toxic substances and some cortin from an alcoholic solution. Lloyd's reagent removes toxic substances together with some cortin from an alcoholic solution. $Al(OH_3)$ acts in a similar fashion.

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How Intravenous Infusions Modify the Water Contents of Tissues.

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To find what factors influence the exchanges of fluid between blood and tissues, muscles and arterial blood were sampled at frequent intervals before, during, and after various acute procedures upon anesthetized cats and dogs. The percentage water contents of the muscles, and occasionally of other tissues, were determined, and blood concentration was measured in parallel by several methods.

[5] McKinley and Fisher, *Am. J. Physiol.*, 1926, **76**, 268.