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Intermediate Oxidation Products of Epinephrine.

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Since Addison made clear the physiological importance of the suprarenal gland, a tremendous number of papers dealing with the physiopathological aspect of the subject have been published, but on the whole comparatively little work has been reported concerning the oxidation products of the active principle. Most chemical investigations have dealt with the oxidation of epinephrine to a pink color with the object of establishing a quantitative chemical assay. Although numerous methods have been reported, only the persulphate oxidation method gives comparable results with those obtained by biological assays. The present work was undertaken with the object of isolating if possible and identifying the chemical constitution of the red oxidation product or products of epinephrine.

Crystalline epinephrine was treated with anhydrous silver oxide in a manner described by Willstätter[1] for the oxidation of catechol to quinone. This procedure necessitated complete absence of water from the reacting substances. Crystalline epinephrine (0.5 gm.) was suspended in methyl alcohol. Three equivalents of silver oxide were added and the mixture shaken for 5 minutes. The mixture was filtered and, after reducing the volume of the filtrate in a vacuum desiccator, crystallization was effected in the cold by the addition of anhydrous ether. A fine red crystalline product separated which decomposed rapidly into a brown amorphous substance in a manner similar to the experience of Willstätter with orthoquinone. More stable crystals were obtained by allowing oxidation to take place in an inert medium such as amylene. The red product crystallized in bright red microscopic needles upon the silver oxide. It was impossible, however, to recover these crystals from various solvents or floating processes without decomposing them. The red product was removed from the silver oxide by dissolving it in methyl alcohol, and its constitution was identified as a mono methyl amino ethanol 3:4 quinone (epinephrine with the 2 hydroxyl groups on the benzene ring oxidized to keto groups) by the method described by Koch and Jackson[2] for the identification of quinone. Mono-

1 Willstätter, R., *Ber. deutsch. Chem. Ges.*, 1904, **37**, 4744.

2 Koch, W., and Jackson, C. L., *Ber. deutsch. Chem. Ges.*, 1898, **31**, 1457.

methylaminoethanol 3:4 quinone has no effect on blood pressure.

It was impossible to oxidize the secondary hydroxyl group in the side chain of the epinephrine molecule without disrupting the benzene ring. The epinephrine product with 3 keto groups (monomethylamino aceto 3:4 quinone) can be obtained however by starting with adrenalone and then oxidizing the catechol group to quinone. Adrenalone was prepared by a method employed by Dziergowski.[3] This product was dissolved in the minimum of 0.1 N HCl and aqueous ammonia added until yellow crystals of adrenalone began to appear. Ammonia was added further while the solution was vigorously stirred. The solution first turned pink, then red and finally a dark red crystalline product separated out upon standing in the cold. The crystals were washed with cold water and dried. The product had no effect on blood pressure. (Found: C, 60.4; H, 5.4; N, 8.0. $C_9H_9NO_3$ requires C, 60.3; H, 5.0; H, 7.8). Monomethylamino aceto 3:4 quinone is more stable than monomethylaminoethanol 3:4 quinone. The same characteristic is shown by epinephrine and adrenalone.

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Effects of Ingested Fats and Sterols on Sterol Metabolism of the White Rat.

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In a study of the effects of the ingestion of plant fats and sterols on the metabolism of the white rat, young litter mates were placed on plant diets consisting of a mixture of soy bean meal, corn oil, agar, starch and the Osborne and Mendel salt mixture. The 2 diets used were so prepared that the protein intake would be practically the same for both groups of rats. The fat content of one diet was 11% as compared with 34% for the other. Both were supplemented with a vitamin B yeast concentrate (Harris), carotene, and viosterol. A record of food intake was kept. The sterol contents of the liver, the remaining tissues, the diets, and the feces were determined gravimetrically by means of the digitonin method. The table shows that

[3] Dziergowski, S. K., *Centralb.*, 1893, **2**, 861.