The Effect of 7-Ketocholesterol on the Rabbit

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Wintersteiner and Bergstrom found that a stream of air passed through a colloidal solution of cholesterol resulted in the production of principally 7-ketocholesterol and 7-hydroxycholesterol (*10*). Kendall, Meyer, and Bevans (*6*) reported that single intravenous injections into rabbits of such oxidized solutions produced lipid droplets within the cells of the intima in 24 hr. Multiple intravenous injections led to an immediate increase of sudanophilic material in the intima, which roughly paralleled the amount of oxidized material injected. In control experiments of these workers, early changes did not result from the administration of unoxidized cholesterol. However, if high plasma cholesterol levels were maintained for several weeks by repeated injections of either unoxidized or oxidized material, there was little difference in the extent or character of the lesions produced.

7-Ketocholesterol was prepared by us according to the method of Windaus, Lettre, and Schenk (*9*). Altschul (*1*) found that when this compound was given to rabbits either orally (in capsules of 0.3 g daily) or percutaneously, as a solution in benzene and vegetable oil (approximately 0.1 g daily), it produced none of the cellular reactions characteristic of the administration of pure cholesterol. However, 7-ketocholesterol administered orally or percutaneously had a definite effect on the liver. Examination showed atrophy of the liver cords and the presence of necrotic areas, numerous giant cells, and an overgrowth of connective tissue and biliary epithelium. In two instances, this organ showed a characteristic "hobnail" surface.

Thus the pathological changes brought about with 7-ketocholesterol did not parallel those found by Kendall *et al.*, using colloidal solutions of cholesterol oxidized according to Wintersteiner and Bergstrom, and therefore presumed to contain chiefly 7-ketocholesterol and 7-hydroxycholesterol. This difference in pathological findings suggested that the effect of administering a mixture of α and β epimers of 7-hydroxycholesterol should be studied, and this is at present under investigation. Also of possible significance is the observation that, under optimum conditions for oxidation, these colloidal solutions contained about 20% unchanged cholesterol (*10*).

Collier and Cox have found that percutaneous administration of approximately 0.1 g of 7-ketocholesterol daily for 64 days resulted in a greatly increased sterol concentration (calculated as cholesterol) in the plasma, as detected by a modification of the Tshugaev reaction (*8*). However, examination of plasma from an animal which received orally 0.3 g of 7-ketocholesterol daily for 40 days showed a comparatively normal sterol level. The plasma of both animals contained only a trace of 7-ketocholesterol, when determined by the micromethod of these workers (*2*). The possibility that liver selectively reduces 7-ketocholesterol to cholesterol, or to a sterol giving a color reaction similar to that of cholesterol when determined by the zinc chloride-acetyl chloride reagent, is now being examined. Of interest in this investigation is the observation that the epimeric 7-hydroxycholesterols, which can be prepared by the selective reduction of the keto group in 7-ketocholesterol (*9*), have been isolated from ox liver in recent years (*3*, *4*, *7*). However, it is not known whether these hydroxycholesterols are true intermediates in sterol metabolism, or only autoxidation products of cholesterol, perhaps formed during the process of extraction (*5*, *11*).

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Survey of Chinese Drugs for Presence of Antibacterial Substances[1]

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In view of recent studies on the production of antibiotic substances by higher plants (*1–6*), it seems interesting to make a survey of drugs commonly used in the practice of Chinese medicine for the presence of antibacterial substances. The so-called Chinese drugs are actually roots, stems, seeds, leaves, or flowers of various higher plants in a very dehydrated state (prepared by special methods). This paper reports the results of such a survey.

To 10–20 g of a drug cut in small pieces, 150 ml of distilled water was added, and the mixture was then boiled slowly for 2–3 hr or longer to a final volume of about 25 ml. (This is the customary way of preparing Chinese medicine, except that ordinary tap water is used instead of distilled water.) After preliminary filtering, the filtrate, which is really a concentrated water extract

[1] This work was carried out in 1945 before departure of the authors for the United States. Since the return of the senior author to China in 1947, some of the experiments were repeated and extended.

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