Cataract Development in Rats Fed Commercial Quercetin.* (26950)

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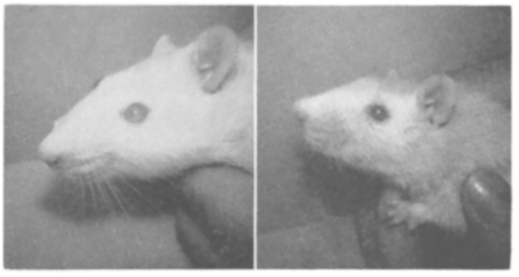
The metabolic fate of quercetin (3,3′,4′,-5,7-pentahydroxy flavone) in animals and its apparent lack of toxicity have been investigated by several research groups (1-5). Recently it has been discovered in this laboratory that a dose of 20 mg or more of commercially purchased quercetin will produce cataracts in eyes of a significant percentage of laboratory rats when administered orally. The effects of purified quercetin and of the impurities found in the commercial quercetin have also been studied.

Methods. Male albino rats, Holtzman strain, 2 months old, were fed a vitamin B complex test diet (Nutritional Biochemicals Corp., Cleveland, Ohio), with complete vitamin fortification for at least one month before use of quercetin. This diet was also continued throughout the test periods. Weighed amounts of the commercial quercetin (Nutritional Biochemicals Corp.) were suspended in U.S.P. syrup, Spec. Grav. 1.313, and administered to each rat by stomach tube.

Results. When a suspension containing 100 mg of the commercial quercetin was put into the stomach of each of 10 rats (3 months old) as a one-dose administration, one rat died within 7 days. Of the remaining 9 rats, 4 developed one cataract each within 4 weeks after receiving the single dose of the commercial quercetin. Microscopic examinations of eye sections confirmed the presence of the cataracts. Vesicular degeneration was noted in the posterior lens capsule and in the body of the lens. An uneven eosinophilia was noted throughout the capsule and body of the lens after staining with hematoxylin and eosin. No changes were noted in the retina or the epithelial area which in non-albino animals is normally pigmented. Two additional rats of this group developed cataracts within 10 weeks after the single dose of quercetin was given. Twelve control rats (6 given syrup, 6 synethic diet only, except that quercetin was not administered) were completely normal after the same length of time.

When a total of 20 mg of the commercial quercetin was administered by stomach tube to each rat of a second group (6 rats, 5 months old) in doses of 5 mg daily for 4 days, 3 of the 6 rats developed cataracts within 6 weeks after the initial dose. No cataracts were found in the controls (6 syrup, 6 synthetic diet only). When a total of 100 mg of the commercial quercetin was put into the stomach of each rat of a third group (8 rats, 6 months old) in doses of 25 mg daily for 4 days, 4 of the 8 rats developed cataracts after 4 weeks. A typical cataract development in this group is shown in the photograph (Fig. 1a) and compared with a normal eye in the other photograph (Fig. 1b).

Using a silicic acid column, chromatographically pure quercetin was obtained. When this pure, crystalline quercetin was administered by stomach tube to rats in



A B

FIG. 1.

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doses (25 mg/day/4 days) as previously described for the experiments using commercial quercetin, no cataracts were found in a group of 6 rats after 3 months following the administration of quercetin.

The mixture of impurities separated from the quercetin on the silicic acid column was eluted as a group and fed to 2 rats. Within 2 weeks, 1 of these 2 rats already exhibited the beginning of cataract development.

Work is now in progress on separation of the 8 or more individual compounds present as impurities in the commercial quercetin and on testing the effect of each compound on development of cataracts.

Summary. When 20 mg or 100 mg of commercial quercetin suspended in U.S.P. syrup was put into the stomach of a rat, either in a single dose or in 4 daily doses of 5 mg or 25 mg respectively, 50% of the animals so treated developed a cataract in one eye within 10 weeks following receipt of the quercetin. No bilateral cataracts were observed. Chromatographically pure quercetin did not cause cataracts under similar conditions.

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Connective Tissue Defect in the Chick Resulting from Copper Deficiency.* (26951)

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Since the observations of Hart *et al.* (1), the primary physiological role of copper has been assumed to be concerned with hemopoiesis. A function in connective tissue metabolism has been suggested by bone deformities that occur in dogs (2) pigs (3) and chickens (4), and by the subcutaneous hemorrhage and abdominal hernias observed in newborn rats (5) when these animals were deprived of dietary copper. Gallagher (4) was unable to produce copper-deficiency anemia in chicks but recently Hill and Matrone (6) have produced anemia in presence of adequate iron. The purpose of the present study was to investigate other aspects of the pathology of copper deficiency in chicks.

Methods. Crossbred Vantress X White Rock chicks were kept in battery brooders which had been coated with an epoxy resin. Eight 4-week trials were run using 10 or 20 chicks per group. The basal diet had the following composition: Non-fat milk solids 55.0 g, sucrose 35.3 g, soybean oil 5.0 g, glycine 1.5 g, L-arginine HCl 1.0 g, DL-methionine 0.5 g, $CaHPO_4$ 1.0 g, NaCl 0.5 g, choline Cl 0.2 g, $MnSO_4 \cdot H_2O$ 31 mg, $FeSO_4 \cdot 7H_2O$ 25 mg, KI 0.3 mg. A vitamin

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