Antitoxic effects of plant fiber[1]

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An extensive series of studies have been conducted during the past 20 years indicating the beneficial effects of alfalfa and other plant fiber-containing materials in counteracting the toxic effects of a number of drugs, chemicals, and food additives when administered at high doses to animals fed highly purified, low-fiber diets (1–9). The protective factor or factors in these fiber-containing materials is distinct from any of the known nutrients. Supplements of purified cellulose in the case of a number of the above toxic agents had a moderate protective effect, but in all cases studied the protective effect of the plant fiber-containing materials was greater than could be accounted for on the basis of their cellulose content per se. These studies were initiated by the observation of Woolley and Krampitz (1) that immature mice fed a purified ration containing 5–10% glucoascorbic acid developed a severe condition characterized by failure of growth, diarrhea, subcutaneous hemorrhages, an unthrifty appearance, alopecia and death. These effects did not occur in mice fed similar doses of glucoascorbic acid in conjunction with a natural food stock ration nor in mice fed the purified diet supplemented with dried grass. Subsequent studies demonstrated that alfalfa meal when incorporated at a 10% level in the diet was similarly effective in counteracting the toxic effects of glucoascorbic acid in the mouse and that the protective effects of alfalfa meal were not due to its content of any known nutrient (2). Similar findings were also obtained in the rat (3). The protective factor or factors in alfalfa was retained in the alfalfa residue fraction (the water-washed pulp remaining after extraction of the juice). Dried alfalfa juice was devoid of activity. Dehydrated rye grass, orchard grass, wheat grass, fescue grass, and oat grass were also potent sources of the active factor or factors. Cellulose per se when incorporated in the purified, glucoascorbic acid-containing diets had a moderate protective effect in both the mouse (2) and rat (3), but its protective effect was considerably less marked than that obtained with the plant fiber-containing materials indicated above.

In 1953 Chow et al. (4) reported that the nonionic surface-active agent polyoxyethylene (20) sorbitan monostearate (Tween 60) when incorporated at levels of 5% or higher in a purified, low-fiber diet induced growth retardation, diarrhea, and other toxic effects when fed to weanling rats but that such adverse effects were counteracted by the concurrent administration of bulk-forming substances. These investigators suggested that the toxic effects of Tween 60 when fed with the purified, low-fiber diet were due to the lack of sufficient residues in the ration to absorb the surface-active agent, which was irritating to the intestinal tract by virtue of its physical properties; and they cited as evidence for this hypothesis their finding that the addition of bulk-forming substances such as celluflour or agar to the diet prevented the occurrence of such toxic effects. Subsequent studies (5) indicated, however, that marked differences exist in the activity of different bulk-forming substances in counteracting the toxic effects of Tween 60 when fed with a purified, low-fiber diet. Immature mice fed a highly purified, low-fiber diet containing 7.5% Tween 60 were found to exhibit a marked

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retardation in growth, diarrhea, an unthrifty appearance, and decreased survival. These effects were largely counteracted by the concurrent administration of alfalfa meal, dehydrated rye grass, orchard grass, wheat grass or fescue grass at a 10% level in the diet or carrageenin, sodium alginate or agar at a 5% level of feeding. Cellulose in the form of Solka-floc or cellophane spangles when fed at a 5% or 10% level prevented diarrhea and promoted survival but were not as active as the substances indicated above in counteracting the retardation in growth. The protective factor or factors in alfalfa was retained in the alfalfa residue fraction. Dried alfalfa juice was without protective effect as was also the case with supplements of the known nutrients. The protective effect of alfalfa meal was also demonstrated in mice fed purified, low-fiber diets containing the nonionic surface-active agent poloxyethylene (40) monostearate (Myrj 52) (5). Similar findings to those reported above for the mouse have also been observed on purified, low-fiber diets containing high levels of Tween 60, Myrj 52 or Tween 20 in the rat (6).

The protective effect of supplements of alfalfa meal has also been demonstrated in rats fed a purified, low-fiber diet containing a toxic level of chlorazanil hydrochloride (7). The latter is a potent, orally active, nonmercurial diuretic which has been effectively employed in Europe and the United States in patients with edema due to congestive heart failure, toxemia of pregnancy, peripheral vascular disease, hepatic cirrhosis, renal disease and other conditions. It is particularly suitable for long-term therapy since with continued administration of the recommended therapeutic dosage disturbances in the concentrations of plasma electrolytes are not induced and the incidence of side effects is low. In some patients, however, an increase in blood nitrogen occurs, particularly at the higher dosage levels. Studies were conducted in which immature rats were fed a toxic level (1.5 g/kg of ration) of chlorazanil hydrochloride in a highly purified, low-fiber diet and the results obtained contrasted to those on similar rations supplemented with alfalfa meal and other supplements. Findings indicated that the above dose of chlorazanil hydrochloride under the conditions of the experiment resulted in a highly significant retardation in weight increment and an increase in serum nonprotein N, urea N, and creatinine. These effects were largely counteracted by the concurrent administration of alfalfa meal at a 20% level in the diet. Supplements of the known nutrients or cellulose per se at a 10% level in the diet were without protective effect (7).

More recently studies have been reported on the beneficial effects of alfalfa meal and other plant fiber-containing materials in counteracting the toxic effects induced by sodium cyclamate when incorporated at a 5% level in a purified, low-fiber diet (8). Immature rats fed the latter ration exhibited a marked retardation in growth, an unthrifty appearance of the fur, varying degrees of alopecia, and extensive diarrhea with watery and mushy stools. Alfalfa meal when incorporated at levels of 10, 15, or 20% in the above ration had a distinct growth-promoting effect which was proportional to the level fed. The protective effect of alfalfa meal was particularly marked at the 15% and 20% levels of supplementation. In rats fed the latter diets the fur appeared smooth and sleek and with the exception of a mild diarrhea and soft but well-formed stools the animals appeared normal in gross appearance. Other plant fiber-containing materials such as wheat bran and desiccated kelp when fed at a 10% level in the diet also had a protective effect. Purified cellulose at a 5 or 10% level of supplementation was also active in counteracting the toxic effects observed on the purified, low-fiber, sodium cyclamate-containing diet but it was less active in this regard than the supplements indicated above (8). Subsequent studies (B. H. Ershoff and W. E. Marshall, unpublished data) indicated that the protective factor or factors in alfalfa was retained in the alfalfa residue fraction and that dried alfalfa juice or alfalfa ash (when fed at a level corresponding to that present in a supplement of 20% alfalfa meal) was devoid of activity. Significant activity exceeding that of a 10% cellulose supplement was also exhibited by other plant fiber-containing materials including blond psyllium seed powder, blond psyllium husk powder, agar, Irish moss powder, gum guar, watercress powder, parsley powder, celery leaf and stalk powder, carrot root powder, sugar cane bagasse, rice straw and

pectin N.F. when incorporated at a 10% level in the diet.

Available data indicate that plant fiber-containing materials are also active in counteracting the toxic effects induced by the red dye amaranth (FD & C Red No. 2) when incorporated at a 5% level in a purified, low-fiber diet (9). Immature rats fed the latter ration exhibited a virtual cessation of growth, an unthrifty appearance of the fur and death within the first 2 weeks of feeding. Supplements of the known nutrients either alone or in combination when incorporated in the above diet had little if any protective effect. The toxic effects were counteracted, however, by alfalfa meal, alfalfa residue, watercress powder or parsley powder when incorporated at a 10% level in the above diet. Purified cellulose at a 10% level of feeding was as active as the supplements indicated above in counteracting the toxic effects of amaranth when incorporated in a purified, low-fiber diet which was not the case when cellulose was fed with purified, low-fiber diets containing glucoascorbic acid, Tween 60, or sodium cyclamate. When administered at a 2% level in the diet, however, which corresponded to the crude fiber content of a 10% alfalfa meal supplement, cellulose per se had little if any protective effect (9). It would appear from these findings that the protective effect of alfalfa meal and the other plant fiber-containing materials indicated above was due, at least in part, to some factor or factors other than their cellulose content per se. It is of interest in this regard that pectin N.F. when fed at a 10% level in the ration was also active although less so than the supplement of 10% cellulose in counteracting amaranth toxicity when incorporated in the purified, low-fiber, amaranth-containing diet.

The studies summarized above indicate that various drugs, chemicals and food additives are highly toxic when fed to rats and mice in conjunction with a purified, low-fiber diet at dosages that are without deleterious effect when fed with diets that are high in dietary fiber. They also indicate that different plant fibers vary significantly in their ability to counteract the toxic effects obtained. These findings may be of considerable public health significance. Painter and Burkitt (10) have pointed out that during the last century due in large part to the refining of flour and other cereals and the increased consumption of sugar at the expense of bread a marked reduction has occurred in the amount of dietary fiber ingested by Western man. In addition there has been a marked decline in the per capita consumption of fresh fruits and vegetables which are also sources of dietary fiber[3] and an increased consumption of fruit juices which are virtually devoid of such fiber. Estimates are that the dietary fiber intake of Western man is now in the neighborhood of 20% of what it was in the mid-19th century and what it is for the rural African today on his native diet. Associated with this reduction in the fiber content of the diet of Western man there has been an accompanying increase in such disorders as diverticulosis, adenomatous polyps, ulcerative colitis, hemorrhoids, and cancer of the rectum and colon, conditions which are virtually nonexistent in populations subsisting on high residue diets (10). In view of the low-fiber diets ingested by so many persons in the United States and other Western countries, serious questions arise as to whether the ingestion of drugs, chemicals, and food additives that may be without deleterious effects when ingested by persons on high-fiber diets may not constitute a hazard to health for a substantial portion of the population of these countries.

An extensive literature is available which has recently been reviewed by Trowell (11, 12) indicating the hypocholesterolemic and antiatherosclerotic effects of certain dietary fibers in experimental animals and man. There is evidence that plant fibers with antitoxic activity may be without hypocholesterolemic activity and that the converse may also be true. Thus low methoxy pectin (i.e., pectin with a

[3] Dietary fiber consists of far more than what is measured by the crude fiber determinations that appear in food composition tables. Crude fiber as defined by the Association of Official Agricultural Chemists is that material which is lost on ignition of the dried residue remaining after digestion with sulfuric acid and sodium hydroxide under specific conditions. It is a measure of the cellulose and lignin content mainly. The term "dietary fiber," however, applies to all plant material resistant to hydrolysis by the digestive enzymes of man (12). Included in this category are not only those substances measured by crude fiber determinations but such substances as pectins, gums, mucilages and a number of hemicelluloses as well.

methoxyl content of 5.0% or less) had marked activity in counteracting the growth retardation and other toxic effects in rats fed a purified, low-fiber diet containing 5% sodium cyclamate (unpublished data) but was without activity in counteracting the increment in plasma and liver cholesterol and liver total lipids induced by cholesterol feeding in the rat (13). Similarly sodium alginate had marked activity in counteracting the growth retardation and other toxic effects in rats fed a purified, low-fiber diet containing 15% Tween 60 (6) but was without activity in counteracting the increment in plasma and liver cholesterol and liver total lipids induced by cholesterol feeding in the rat (14). Conversely, locust bean gum which had marked activity as a hypocholesterolemic agent in the rat (15) was virtually devoid of activity in counteracting the toxic effects induced by sodium cyclamate when incorporated at 5% level in a purified, low-fiber diet in the rat (Ershoff and Marshall, unpublished data).

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