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Special Article

The Vitamin Fraud in Cancer Quackery

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THE ATTEMPTED EXPLOITATION of the cyanogenic glucosides, particularly amygdalin—under the name Laetrile—in the treatment of cancer has a long history.

Amygdalin was first isolated from bitter almonds by the French chemists Robiquet and Boutron-Charlard in 1830. Liebig and Wohler observed that amygdalin was hydrolyzed with the evolution of benzaldehyde and hydrogen cyanide by an enzyme preparation from bitter almonds later named emulsin.[1] Later work showed that emulsin was an enzyme mixture containing among others, the specific enzymes beta-D-glucosidase and beta-oxynitrilase. Beta-D-glucosidase specifically hydrolyzes the beta-D-glucoside linkage. Liberation of benzaldehyde and cyanide from the released mandelonitrile is catalyzed by beta-oxynitrilase.

The two common laetriles are amygdalin and prunasin (Figure 1). Prunasin contains one less glucose molecule in beta-D-glucoside linkage.

When these compounds are cleaved by the enzyme beta-glucosidase there are liberated the sugar, glucose, and the cyanohydrin of benzaldehyde (mandelonitrile). As shown in Figure 2, the mandelonitrile decomposes to a slight degree spontaneously to benzaldehyde and hydrocyanic acid (HCN).

Laetrile has been promoted as an anticancer agent for many years. The Krebses (E. T. Krebs, Sr. and E. T. Krebs, Jr.) isolated a partially purified preparation from aqueous extracts of defatted ground seeds (U.S. Patent 2,464,240 [1949]). In recent years pure amygdalin, isolated from apricot kernels, is being used, legally in many foreign countries and certain of the states of the United States, and illegally in California.

In 1953, the Cancer Commission of the California Medical Association investigated the claims made for the use of Laetrile in cancer treatment and condemned its use. In 1959 the California Legislature passed Senate Bill 194, to provide a means for combating medical quackery in the diagnosis and treatment of cancer. On authority of this statute the use of Laetrile was made illegal. However, illegal treatment has continued and in recent years the traffic in Laetrile has grown enormously.

Purported Rationale for Laetrile Effect

As noted, the catalytic cleavage of amygdalin or prunasin by the enzyme beta-glucosidase liberates mandelonitrile, which decomposes spontaneously into benzaldehyde and cyanide. The cyanide is presumed to kill cancer cells, but not normal tissue, because in the latter there is postulated to be present large amounts of the enzyme thiosulphate transferase (rhodanese) which converts the cyanide to the less toxic thiocyanate. Cancer tissue is presumed to be rich in beta-glucosidase.[2a]

There are several flaws in this hypothesis:

- The available information shows the presence of only traces of beta-glucosidase in animal tissues and even less in amount in experimental tumors than in such organs as liver and kidney.[2b]
- The beta-glucosidase values reported for tumor tissue give a false picture, since the substrate commonly employed to test for this enzyme was *p*-nitrophenyl-β-D-glucoside. This compound has been observed in the laboratory of Dr. E. Conn at the University of California, Davis, to be an order of magnitude more active as a substrate

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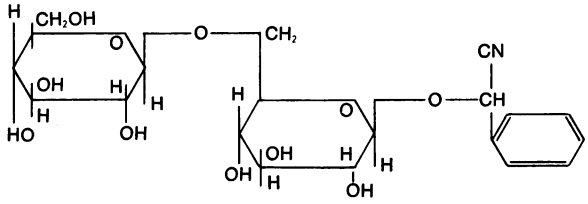
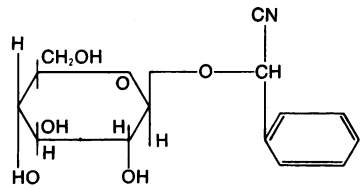


Amygdalin (Mandelonitrile-β-D-glucose-β-D-glucoside)



Prunasin (D[levo]-mandelonitrile-β-glucoside)

Figure 1.—Chemical structures of the two common laetriles, amygdalin (top) and prunasin (bottom).

than amygdalin or prunasin when all are subjected to the action of glucosidase from liver.

- There is no evidence that there is any pronounced differential between the rhodanese content of comparable normal and cancerous tissue.[2b,2c]

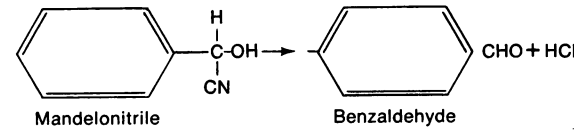
There has been much shifting of ground by E. T. Krebs, Jr. to bolster the claim for Laetrile. One of these efforts was the claim that upon ingestion, amygdalin was hydrolyzed to mandelonitrile and the latter was transported intact to the liver where it was converted to the beta-glucuronide through the action of beta-glucuronidase. The mandelonitrile-beta-glucuronide was then supposed to be carried to cancer tissue and there again hydrolyzed by beta-glucuronidase to mandelonitrile.[3] This absurd proposition was stimulated by the publications of Fishman and Anlyan[4,5] that cancer tissue was rich in beta-glucuronidase.

In an earlier period it was assumed that laetriles were hydrolyzed by the enzyme beta-glucuronidase. This of course is erroneous; instead laetriles are specific substrates for beta-glucosidase because of their beta-D-glucoside bonding.

The Vitamin Theory—Alleged Vitamin B_{17}

In 1970 by a "brilliant" stroke, E. T. Krebs, Jr.[6] transformed the cyanogenic glycosides into a vitamin—a so-called antineoplastic vitamin B_{17}. In the following we will demonstrate the falseness of the claim that the cyanogenic glycosides have any properties akin to the known vitamins.

At a time when there is a considerable revolt against processed foods, and many individuals are receptive to almost any claim of the virtues of "natural" nutrition, the vitamin B_{17} claim has had



Mandelonitrile Benzaldehyde

Figure 2.—Mandelonitrile, liberated when amygdalin or prunasin is cleaved by the enzyme beta-glucosidase, which decomposes spontaneously into benzaldehyde and hydrocyanic acid.

a tremendous impact. Marketing of ground apricot kernels has sprung up and apparently is flourishing. Consequently, the claim for the anticancer properties of Laetrile has taken on added acceptance in some circles.

The claim of E. T. Krebs, Jr. that beta-cyanogenetic glucosides (laetriles), or *nitrilosides* as he terms them, are vitamins—specifically designated as vitamin B_{17}—and that a deficiency of this alleged vitamin is the cause of cancer is examined below and shown to be only a figment of his imagination.

What is a Vitamin?

A vitamin may be defined on the basis of several properties:

- It is a nutritional component of organic composition required in small amounts for the complete health and well-being of the organism.
- Vitamins are not utilized primarily to supply energy or as a source of structural tissue components of the body.
- A vitamin functions to promote a physiological process or processes vital to the continued existence of the organism.
- A vitamin can not be synthesized by the cells or the organism and must be supplied de novo.
- In man and in other mammals, deficiency of a specific vitamin is the cause of certain rather well-defined diseases. These include scurvy, beri beri, pellagra, pernicious anemia and rickets. These diseases are prevented or cured by addition of the appropriate vitamin.

Vitamins that are essential dietary ingredients for certain animal species may not be such for other animal species. One example of this is vitamin C (ascorbic acid) which is essential for man and for guinea pigs but not for most other mammals. The reason for this is that man and the guinea pig have lost the enzymatic machinery required for the synthesis of vitamin C, while this still persists in most other mammals.

Herbivores do not require the ingestion of vitamins in their feed, because of vast numbers of

bacteria present in their rumen. These bacteria can synthesize vitamins that may be lacking in the feed.

The claim that the beta-cyanogenic glycosides represent a new, hitherto unrecognized water soluble vitamin (vitamin B_{17}) is refuted by the following facts.

- No evidence has ever been adduced that laetriles are essential nutritional components.
- Laetriles have never been shown to promote any physiological process vital to the continued existence of any living organism.
- No specific disease has been associated with a lack of a laetrile in any animal. Since experimental animals (mice, rats, guinea pigs) have been maintained in good health over a number of generations on synthetic diets of pure chemical components, but containing no laetriles, it is evident that lack of this material is not associated with any disease.[7,8*]
- The tissues of animal bodies contain enzymes that can decompose all of the usual constituents of foodstuffs and thus form decomposition products that can be readily eliminated. The tissues of the body contain such minute amounts of the enzyme beta-glucosidase, the only enzyme that can decompose laetriles, that these compounds probably are not extensively broken down when introduced parenterally and are probably excreted mainly intact in the urine. When ingested by mouth the laetriles are decomposed by beta-glucosidase present in the microbial population of the intestinal tract and the breakdown products are disposed of in a manner normal for each component. This is the reason why the laetriles taken orally are much more poisonous than when injected. It is then that highly poisonous cyanide is liberated.
- One of the fundamental properties of a vitamin is that it has a unique physiological function that can not be performed by any other class of compounds. No evidence has been adduced that laetriles have any such physiological function. The claim that laetriles have the property of a vitamin (so-called vitamin B_{17}) therefore is not supported by any valid scientific evidence.

Other statements of dubious validity have been made in attempting to establish physiological functions for cyanogenic glycosides:

- It has been said that cyanogenic glycosides could account for the thiocyanate of body fluids. This is not a unique property, since any source of cyanide formed in the body (and some are known) can be converted to thiocyanate through the action of rhodanese. For example, it is well known that smoking increases the excretion of thiocyanate.
- It has been stated that cyanogenic glycosides might be the source of the cyanide that goes to the formation of cyanocobalamin. Cyanocobalamin is not the active form of vitamin B_{12}. Actually it is an artifact formed from the physiologically active hydrocobalamin during the isolation of vitamin B_{12}.

The above suggested properties, of course, have no bearing on the alleged vitamin nature of the cyanogenic glycosides since they can be caused by any source of cyanide.

Vitamins and Cancer

Is there some special relationship between vitamins and cancer? There are no valid grounds to believe there is. After many years' search for a unique difference in metabolism between normal and neoplastic cells, none has been found—except for quantitative differences in rates of certain metabolic reactions. Cancer cells, like normal cells, require the known essential nutrients to grow and proliferate. Cells with a high rate of turnover are more susceptible to a nutritional deficiency than nonproliferating or slowly proliferating cells.

The nutritional studies of an earlier period relating to cancer have been reviewed by several writers.[9,10] The induction time of spontaneous mammary carcinomas as well as of certain other tumors in mice was found to be lengthened by dietary restrictions including restriction of certain of the B vitamins. However, this was shown not to be a direct effect, but rather was due to the production of abnormalities in estrogen metabolism.

Deficiency of various vitamins of the B group inhibits growth and may lead to the destruction of rapidly growing neoplasms, as is also true for normal cells. This has been proved most strikingly by the administration of certain vitamin analogues which produce a profound vitamin deficiency by interfering with the normal utilization of the vitamin for its appropriate function.[11-15]

For example, methotrexate (amethopterin), one of the most useful anticancer drugs, exerts its curative effect by interfering with the normal cellular functions of the vitamin folic acid.[11] This analogue is, of course, also toxic to body cells with a high rate of turnover, namely the hema-

*Synthetic diets free of cyanogenic glycosides have been employed in nutritional research for over 40 years. The references given represent only one example of numerous synthetic diets published in nutritional journals.

topoietic system, intestinal mucosa and dermis. By a proper regimen that permits the regeneration of normal, affected tissues, methotrexate is useful in the treatment of a variety of neoplasms.

Other examples of the inhibition of the growth of experimental cancers are by isoriboflavin, an antagonist of riboflavin; deoxypyridoxine, an antagonist of pyridoxine and pyrithiamine, an antagonist of thiamine. These agents have not found use in cancer treatment because there is only a small differential between the toxic action on cancer and normal cells.

Could Cyanide Be a Useful Agent for the Eradication of Cancer?

If cyanide was formed in the body, either through cleavage of amygdalin or by direct administration, would it be expected to have a specific cytotoxic effect on cancer tissue? The answer is no. Dating almost from the beginning of this century experiments have been made on the effects of injecting cyanide into cancer-bearing rodents or of maintaining such animals in an atmosphere containing a fixed concentration of HCN gas.[16-19] Increases in survival time of the treated cancer-bearing animals were observed, but the animals also developed erythema, edema and necrosis of the extremities.[18] The general conclusion was that the effective doses were too close to the lethal dose to be of practical use.[16-19]

Brown et al[20] administered cyanide along with anesthetic to patients with uterine tumors directly to the tumor and observed no improvement.

In experiments that have been carried out with amygdalin, this compound has been administered along with beta-glucosidase. The results have been an increased toxicity with no evidence of improvement of anticancer activity.

Summary

The claim that laetrile (amygdalin) has the properties of a vitamin (so-called vitamin B_{17}) is shown to be false by the normal properties characteristic of vitamins. There is no substantial evidence that any vitamin prevents the development of, or has a beneficial effect in the treatment of neoplasms.

The published literature does not support the assumption that cyanide, presumably liberated on the enzymatic decomposition of laetrile, has a specific action on neoplastic cells.

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