Low-cal aspartame: The new kid in town

Move over, saccharin, and make way for aspartame. After seven years of controversy and despite the misgivings last October of a special board of inquiry, the Food and Drug Administration recently gave G. D. Searle & Company of Skokie, Ill., the go-ahead to market this new low-calorie sweetener that is 180 times sweeter than table sugar.

The new sweetener consists of two amino acids — aspartic acid and phenylalanine — and methyl alcohol. It has been approved for use both as a free-flowing table sugar substitute and as an additive in cold cereals, drink mixes, puddings, chewing gums, dairy products and instant coffee and tea. (Because Searle did not initially seek approval for use of aspartame in liquid products, its sweetener cannot yet encroach upon saccharin's diet soft drink territory.)

FDA first approved aspartame for such uses in July 1974. The next month, however, psychiatrist John W. Olney of Washington University in St. Louis and Washington-based lawyer James S. Turner objected to that approval in part due to scientific data suggestive of aspartame's potential for causing brain tumors in laboratory rats.

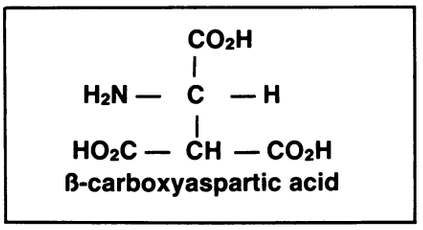
In January 1980 a three-member board of inquiry — chaired by Walle J. H. Nauta of Massachusetts Institute of Technology in Cambridge — was established to consider the question of brain tumors. The board also reviewed data to determine whether use of aspartame could cause nerve cell death — there is evidence that acidic amino acids are potential neurotoxins — and increased mental retardation in persons with undiagnosed phenylketonuria.

Phenylketonuria — a condition that strikes about one in 15,000 infants — is characterized by the victim's inability to properly metabolize phenylalanine. If untreated, this condition causes mental retardation. Since phenylalanine is one of the building blocks of aspartame, Olney and Turner were concerned that undiagnosed phenylketonurics could suffer additional retardation if they used the sweetener. The board, however, decided on the basis of a projected mean phenylalanine intake from aspartame of 3 milligrams per kilogram per day that the sweetener could not significantly increase the risk of mental retardation in unidentified phenylketonurics. Also, the risk of nervous system damage was deemed "negligible."

But one concern could not be alleviated — that of brain tumors. In October, 1980, the board concluded that approval of aspartame should be withheld until further experiments could resolve this issue (SN: 11/8/80, p. 293).

Now, on the basis of one more long-term feeding test (by H. Ishii of the Japanese company Ajinmoto) and a re-evaluation of Searle's data, FDA has approved use of aspartame. Products containing aspartame — which will bear a warning to phenylketonurics — are expected on the market by the end of the year. □

Another amino acid isolated in bacteria



ß-carboxyaspartic acid

A previously unknown amino acid, beta-carboxyaspartic acid (Asa), has been discovered in bacteria. The biological function of the amino acid, the amounts of it present in proteins and its prevalence in organisms more complex than bacteria have yet to be determined. Nonetheless, its structural similarity to gamma-carboxyglutamic acid (Gla) — an amino acid implicated in blood clotting and kidney functions in humans — has led University of Colorado scientists to theorize that Asa may play a major biological role. The story of the discovery is in the July 1 JOURNAL OF THE AMERICAN CHEMICAL SOCIETY.

While sifting through proteins in the ribosomes of the common bacterium *Escherichia coli,* John J. Van Buskirk and Wolff M. Kirsch of the University of Colorado at Denver noticed that acid-catalyzed hydrolysis of those proteins yielded slightly greater amounts of aspartic acid than did base-catalyzed hydrolysis. Although the difference in amounts was so tiny that it had been overlooked in past investigations, the two researchers suspected that a previously unknown amino acid was responsible for the aspartic acid surplus.

M. Robert Christy and Tad H. Koch of the University of Colorado at Boulder then confirmed the theory by synthesizing authentic Asa and characterizing its protein hydrolysis products through mass spectrometry. Further comparisons indicated that the chemical from the bacteria and the synthetic Asa were identical.

Now the researchers are eager to determine whether the biological activity of Asa is similar to that of Gla. While a mere addition of carbon and a couple of hydrogen atoms distinguishes Gla from Asa structurally, Gla seems less reactive than the newly-discovered Asa. First isolated in 1974, Gla appears to play a role in the conversion of prothrombin to thrombin, an enzyme important in blood clotting at the site of an open wound. And because vitamin K interacts with Gla to aid in blood clot formation, future, more detailed comparisions of Asa and Gla may shine light on this vitamin's mode of action.

Meanwhile, the Colorado researchers are planning to test for the "new" amino acid in human cell cultures. "I believe that [Asa] is present in mammalian ribosomal cells too," says Van Buskirk, "but we don't know that yet." □

Emotions and sudden death

Numerous case reports attest to the fact that intense emotional upsets can kill, and kill quickly. But how? Researchers at Brigham and Women's Hospital in Boston suggest that they may do so by triggering fatal ventricular fibrillation.

Ventricular fibrillation is an abnormally rapid, chaotic beating of the heart ventricles. If not corrected within minutes, fibrillation can lead to heart failure and death. Because sudden cardiac-related deaths now are known to be frequently caused by ventricular fibrillation — often in the absence of a heart attack (death to a segment of heart muscle) or of other signs of heart disease — Peter Reich and co-workers investigated whether intense emotional disturbances can trigger such fatal ventricular arrhythmias. Their retrospective study, published in the July 17 JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION, involved determining the emotional states of 117 patients who had survived life-threatening ventricular fibrillation.

Patients were classified according to whether they had heart disease or not. Then each patient was interviewed independently by a psychiatrist and by a cardiologist to learn what events and psychological states each had experienced during the 24 hours preceding the ventricular fibrillation episode. Details were also obtained from witnesses.

Of the 117 patients, 25 (or 21 percent) were found to have had acute psychological disturbances during the 24 hours preceding their fibrillation episodes. Anger, acute depression, fear, anticipatory excitement and grief, were the most commonly reported symptoms. These emotional states had been sparked by interpersonal conflicts, public humiliation, threat of or actual marital separation, bereavement, business failure and, in one instance, nightmares. In 15 of the 25 patients, disturbances had lasted one hour prior to onset of the fibrillation episode; in seven patients, six hours; and in the remaining three, 12 to 24 hours. In addition, compared with the other 92, these 25 patients showed far less evidence of heart disease, suggesting that their ventricular fibrillation episodes had been set off largely by emotions alone, not by emotions plus heart disease. The researchers say that this is indirect evidence that emotional stress may contribute to ventricular fibrillation in susceptible patients. □