

/A RATIONALE FOR THE USE OF ASPARTAME AS A SUGAR
SUBSTITUTE IN THE POSSIBLE REDUCTION OF DENTAL CARIES/

by

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I. MICROBIOLOGICAL ASPECTS OF DENTAL CARIES

A. Dental Caries - An Epidemiological Model

According to the epidemiological model, a disease results from the interaction of three primary factors: the host, the agent or recruiting factor, and the environmental influences. In addition, several secondary factors may also affect the rate of progression of a disease. Therefore, a disease is viewed as a product of primary and secondary interactions. This concept of viewing a disease process can be applied to dental caries.

1. The Primary Factors

Dental caries (decay) is by far the most widespread disease in advanced societies throughout the world (Grenby, 1984). It results from the interaction between three primary factors: a susceptible host tissue, the tooth; microflora with a cariogenic potential; and a suitable local substrate to meet the energy and nutritional requirements of the pathodontic flora. In the dental caries process, the tooth is destroyed by the organic acids, chelating agents, and the proteolytic enzymes secreted by the cariogenic oral flora which is localized in specific sites on teeth. The local substrate provides the nutritional and energy requirements for the bacteria.

The experimental evidence in support of bacteria and a suitable local substrate as prerequisites for dental caries is overwhelming. The resistance of the tooth determines the overall effect of the attack. Although some discrepancy exists as to how and which microorganisms produce carious lesions, it is generally accepted that caries can not occur without microorganisms.

In their study, McClure and Hewitt (1946) demonstrated that an antibiotic, penicillin, fed to animals significantly reduced experimentally induced caries. This experiment suggested that bacteria were involved in caries. In consequence, the range of suspected microorganisms was narrowed down to gram-positive bacteria, the primary target within the antimicrobial spectrum of penicillin.

The classical germfree animal studies of Orland et al. (1954) firmly established the principle that dental caries is a bacterial infection. The studies demonstrated that germfree rats on a highly cariogenic diet containing sucrose did not develop caries. When the gnotobiotic rats on the same diet were infected with one or more pure cultures of microorganisms, carious lesions developed. These findings were confirmed by various independent investigators. Thus, the debate about the role of bacteria in dental caries was finally settled-

dental caries is a disease caused by oral bacteria.

New experiments were initiated to determine the specificity of microorganisms involved in the initiation of dental caries. These studies were conducted by introducing a limited, defined flora into gnotobiotic animals in an attempt to produce caries.

The term gnotobiotic animals refers to an animal with a known microbiota (Greek: gnosis = positive knowledge). Gnotobiote includes both germfree or axenic (free from foreign organisms) animals and ex-germfree animals deliberately inoculated with one or more types of microbes for experimental purposes. Conventional animals deprived of a specific segment of their microflora by antibiotics are not included since the remaining microflora can not be precisely defined.

Subsequently, several organisms have been shown capable of inducing dental caries in the gnotobiotic animal. These include Streptococcus mutans (several strains), a S. salivarius strain, a S. milleri strain, S. sanguis (several strains), Peptostreptococcus intermedius, a Lactobacillus acidophilus strain, a L. casei strain, Actinomyces viscosus, and A. naeslundii. However, not all of these organisms have the same capacity to induce caries formation in the animal test system.

The role of microorganisms in caries has been

clarified by studies on gnotobiotic animals. Fitzgerald (1968) summarizes these findings as follows:

- . Microorganisms are a prerequisite for caries initiation.
- . A single type of microorganism (for example, Enterococcus strain) is capable of inducing caries.
- . The ability to produce acid is a prerequisite for caries induction but not all acid-producing (acidogenic) organisms are cariogenic.
- . Streptococcus strains that are capable of inducing caries are also able to synthesize extracellular dextrans or levans. Not all strains that produce extracellular polysaccharides are capable of caries induction.
- . Organisms vary greatly in their capacity (virulence) to induce caries; comparative virulence can not be deduced at present with certainty.

2. The Secondary Factors

Salivary composition and flow rate, oral hygiene, and diet influence the caries process. These secondary factors can affect one or a combination of the following: increase or reduce the tooth (host) resistance to dental caries; increase or decrease the

quantity and quality of the pathodontic flora; or, increase or reduce the cariogenicity of the local substrate.

Saliva serves many functions: cleansing effect, buffering capacity, provision of an environment saturated with calcium phosphate, and antibacterial action. Although all these characteristics influence the rapidity at which caries develop, saliva does not play such an essential role for caries initiation as organisms, local substrate, and teeth do. The same can be said about oral hygiene. Even though oral hygiene affects caries, it is not a primary factor in caries initiation.

The interactions between primary and secondary factors are illustrated in Figure 1 and are summarized in Table 1 .

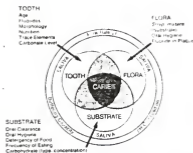


Fig. 1. Diagrammatic representation of the interplay between primary and secondary factors in the caries etiology. (Nikiforuk, 1985).

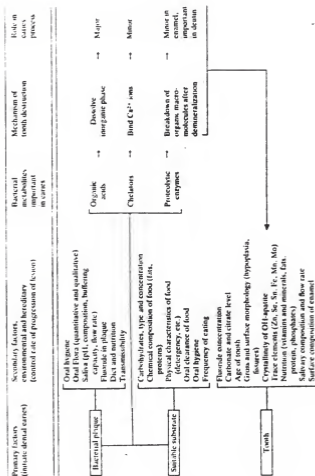


Table 1. The Determinants of Dental Caries (Nikiforuk, 1985).

B. Dental Plaque

Dental Plaque forms immediately after the erupted tooth is exposed to saliva in the mouth. There are three phases to this cycle: (1) the acquired pellicle formation, (2) plaque formation, and (3) calculus formation.

1. The Acquired Pellicle

The acquired pellicle (AP) is a thin amorphous film composed mainly of glycoproteins which form immediately after a tooth surface comes in contact with saliva. Enzymes, immunoglobulins, organic, and inorganic components of saliva are also present in the acquired pellicle. The chemical structure of the glycoproteins is a key factor in the bacterial attachment to the pellicle and it also influence the nature of the colonizing bacteria (van Houte et al., 1970).

Initially, the AP is free of bacteria; however, it requires only about two hours for the pellicle to build to its maximum thickness (Baier et al., 1977). Although a transitory and solitary structure, the acquired pellicle is very important since bacterial colonization is dependent on its preexistence. Some exceptions to this rule have been noted, with the bacteria attaching directly onto the tooth surface (Frank and Brendel, 1966).

The pellicle is called bacterial plaque the moment that bacterial colonization begins (Osterberg et al., 1976). Research suggests that the pellicle is still present between the new bacterial plaque and the tooth surface, and it probably acts as a selective membrane for the acids diffusing from the plaque to the tooth surface (Frank and Brendel, 1966). It may also limit selectively the movement of salivary ions involved in the remineralization of the teeth (Tinanoff et al., 1976).

2. Plaque Formation

Dental plaque is an adherent film of saliva, bacteria, and their end-products which remains fixed to tooth surface despite the muscular action of tongue, lip, or cheek (Alexander et al., 1969). Its formation depends on several factors: (1) the number and type of bacteria available, (2) tooth surface, (3) the strong affinity of the bacteria for the pellicle or plaque, and (4) the personal oral hygiene of the host.

The bacterial colonization of the plaque follows a predictable sequence. The primary plaque colonizers are mainly aerobic gram-positive organisms such as streptococci and lactobacilli. They appear shortly after plaque formation (van Houte and Green, 1974). During the first 48 hours, single larger colonies expand and merge

into larger colonies. Aided by the nutrients contained in the saliva and the host intake, reproduction and metabolic activities increase actively (Selvig, 1970; Tanzer and Johnson, 1976). As the process continues and metabolic end-products accumulate, the secondary plaque colonizers arrive, and are incorporated into the plaque. These new invaders are mostly gram-negative organisms (Lie, 1979; Ritz, 1967). The vibrios, filamentous organisms, and spirochaetes are found in this group (Loe et al., 1965). The dental plaque thickens limiting the diffusion of oxygen; therefore, the organisms in the deeper part of the plaque are either facultative or obligate anaerobes (Ritz, 1967).

Plaque composition changes rapidly during the first five days; then, it slows and become stable by the 21st day (Howell et al., 1965). However, factors such as saliva flow, muscular action and tooth-brushing cause continuous remodeling of the bacterial and intercellular phases of plaque making a population equilibrium quite doubtful.

The metabolic activities created by the bacterial plaque are quite extensive. The total mass of the plaque doubles in about two days. Bacterial interaction occurs, as it may be expected, since a large number of microorganisms are competing for a limited amount of nutrients, while releasing their different end-products

into the environment (Loesche, 1968).

The number and types of bacteria present in the mouth change from time to time within any one individual. Streptococci and actinomycetes are the only two genera found almost universally in the mouth of men and animals. Also, the bacterial end-products are as diverse in chemical structure as ammonia and hydrogen sulfide, and acids, such as lactic acid, acetic, and propionic acids (Geddes, 1975). As the volume of acids released into the oral cavity increases, the pH drops rapidly from around 7.0 to 4.0 - 4.5; enamel demineralization begins between pH 5.5 and 5.0. Subsequently, exotoxins and endotoxins are released into the environment with damaging effects for the plaque inhabitants and the cells of the host.

Acidogenic microorganisms, such as Streptococcus mutans, produce acid (Stephan, 1940), an intercellular polysaccharide, and the extracellular polysaccharides glucan (dextran) (Critchley et al., 1967), and fructan (levan) (McDougall, 1964), after exposure to sucrose. The glucans help in the attachment of the bacteria to the teeth; whereas, fructans act as a source of energy. The glucans and the fructans, along with other substances and bacterial end-products make up the intercellular matrix.

a. Attachment of the bacteria

Rolla (1977) explained the specific adsorption of glycoproteins onto the teeth, and the subsequent adsorption of bacteria into the pellicle as a consequence of electrostatic interactions. Adsorption of bacteria occurs into specific binding sites of the glycoproteins making up the pellicle; the rate of adsorption varies according to the type of bacteria as well as the glycoprotein. Glycans provide a secondary means of attachment. Bacteria not adhering to either the pellicle or to the glucans will adhere to a similar or dissimilar bacteria in the plaque.

3. Calculus Formation

As the plaque thickens, the deeper areas begin to mineralize. This mineralization of the plaque is termed calculus, or tartar. Two kinds of mineralization are observed: supragingival and subgingival. Differences exist between these two types of calculus. The supragingival calculus appears as yellow-to-whitish mass, it has a moderately hard texture, and the shape of the mass is determined by the anatomy of the tooth, contour of the gingival margin and pressure of tongue, lips and cheeks. On the other hand, the subgingival calculus exhibits a gray-to-black color, is dense and hard, and is flattened to conform with the pressure of

the free gingiva. The darker color may be due to bacteria such as Candida niger, or it may be due to hemorrhagic exudate.

C. The Carious Lesion

Dental caries is a localized, posteruptive pathological process of external origin involving the destruction of hard tooth tissues, which if continued, results in the formation of a cavity (Harris and Christen, 1987). The morphology of the tooth dictates to a great extent the sites of development for the carious lesions. In general, carious lesions occur in three areas of the tooth: (1) pit and fissure caries, which are found mainly on the occlusal surfaces of posterior teeth, as well as lingual pits of maxillary incisors; (2) smooth surface caries, which arise on enamel surfaces other than at pits and fissures; and (3) root surface caries, which involve any surface of the root (Jordon and Sumney, 1973).

Various theories for caries development have been considered, such as the acidogenic theory (Miller's chemico-parasitic theory), in which the acid-induced demineralization is the initial causative factor, with a subsequent invasion by proteolytic bacteria, which destroy the protein components of the teeth; (2) proteolytic theory, in which destruction of the protein

matrix occurs before the mineral components of the teeth are destroyed by the bacterial acids; and (3) chelation theory, in which chelates destroy the mineral phase, followed by bacterial destruction of the organic matrix.

Caries may develop over a period of months or even years. During the progress of the lesion, alternate periods of demineralization and remineralization occur simultaneously without any loss of tooth mass. The lesion occurs when the rate of demineralization exceeds the rate of remineralization over a period of time.

Immediately after a lesion develops, the stability of the bacterial population in the plaque alters, and a large number of chemical changes occur rapidly. The aciduric environment often eliminates, or halts the continuous colonization of the plaque by many microorganisms. Some bacteria, such as Streptococcus mutans, release bacteriocin, a toxic agent for other oral cavity inhabitants, in order to secure a protected niche for themselves. Further changes occur in the environment, bacterial population, and tooth structure as the carious lesion continue its progress.

D. The Cariogenic Bacteria

Orland et al. (1954) demonstrated that dental decay was a transmissible and infectious disease caused by bacteria. Later, Keyes (1960) investigated the infection

potential of various organisms in experimental animals. Although many of the organisms inhabiting the plaque are involved in tooth demineralization, not all organisms are equally cariogenic. In fact, many bacteria do not induce caries. At birth, the oral cavity is sterile, but within 6 to 10 hours an aerobic flora develops. Streptococci are among the first bacteria to appear (Zinner and Jablon, 1969). Colonizing bacteria may originate from many external sources - from the air, from hospital personnel, or from close contact with the mother, as demonstrated by Kohler and Bratthall (1978) . Since competition with other organisms is nonexistent, these first bacterial populations establish their niches without major difficulties. When teeth erupt, these bacterial populations contribute to the formation of plaque. Although many microorganisms inhabit the plaque and are involved in cariogenesis, at this time three genera are of special interest: (1) the streptococci, especially S. mutans (Michalek et al., 1977); (2) the lactobacilli, especially L. casei (Bowen et al., 1976); and the actinomycetes, especially A. viscosus (Jordan et al., 1972) and A. naeslundii (Socransky et al., 1970). S. mutans is usually associated with the initiation of smooth surface caries; the lactobacilli are present in pit and fissures caries, while the actinomycetes are associated with root surface caries.

All these microorganisms are acidogenic. In the case of S. mutans, the damage is due to the production of lactic acid, although other acids such as butyric and propionic are present. If the pH of the plaque drops below approximately 5.5, dissolution of the enamel may occur, leading to the formation of a carious lesion.

II. ROLE OF SUCROSE IN CARIES FORMATION

The term sugar applies both to monosaccharides (simple sugars), of which glucose, fructose, and galactose are most common, and disaccharides (two simple sugar molecules linked together) such as sucrose, lactose, and maltose. Sucrose is a disaccharide composed of one glucose linked to one fructose unit.

Sweeteners can be either caloric or non-caloric (low in calories). Caloric sweeteners include monosaccharides and disaccharides, corn syrup, and other sweeteners such as the polyols (sugar alcohols). The two most popular non-caloric sweeteners are saccharin and aspartame. There are several promising new non-caloric sweeteners now in use in other parts of the world and are being studied for potential use in the American market. Two of these, like aspartame, are protein sweeteners: (1) miraculin, and (2) monellin.

A. Sweet Taste

Although it is difficult to determine whether taste is genetically linked, acquired in utero, or part of a learning process influenced by stimuli during infancy, childhood or adulthood (Weiffenbach, 1978), there is evidence of an innate desire for sweets in humans. Taste buds are already present in the four-month old fetus

(Mandel, 1979). An injection of sweetening agents into the amniotic fluid of the mother results in an increased rate of swallowing by the five-month old fetus (Maller and Desor, 1973). Newborn infants exhibit taste preference for sucrose, and their taste cells are more responsive to sucrose than to other sugars. Likewise, studies with adults have demonstrated that a preference for sweet relative to non-sweet is an "unlearned preference present from birth ... unaltered from birth through adulthood" (Desor et al., 1977). Whether it is simply a pleasurable taste or a true metabolic need is not known.

The desire for sweet taste is mostly satisfied by sweeteners containing calories and carbohydrates. In consequence, sucrose constitutes over 15 % of the per capita caloric intake of the population of the United States. Currently, the advent of new non-caloric sweeteners provides an alternative to sucrose while fulfilling the consumers desire for sweets without losing control of their diets.

B. The Historical Importance of Sweeteners

The desire for sweetness has a long history, as illustrated by a 20,000 year-old painting in a cave at Arana (Spain) showing a neolithic man robbing a wild bee's nest of honey, a natural sugar concentrate.

Drawings in Egyptian tombs illustrate beekeeping practices for honey production as early as 2000 BC (Koivistoinen and Hyvonen, 1985).

Cultivating sugarcane began in southeast Asia, India, and China around 100 BC. Sugarcane juice prepared by pressing was well known in ancient Greece and Rome, but the Arabs developed the first process for refining sugarcane into sucrose. Sugarcane was widely cultivated in Southern Europe during the thirteenth century, and the practice eventually spread to the New World.

Bleeding the sap of the sugar maple tree was practiced by the North American Indians long before the arrival of the Europeans to the continent. The sugar in the mature sugar maple tree is almost exclusively sucrose.

Around 1910, sweeteners made from corn starch were introduced as substitutes for sucrose. The sugars derived from corn starch, mostly glucose, are less sweet than sucrose, and this created a problem in identity as well as restrictions on their use. The introduction of new technology has resulted in a process able to convert the glucose contained in corn starch to a high fructose corn syrup (HFCS). Because fructose is twice as sweet as glucose, its use has been widely accepted in the Food Industry. Most recently, non-caloric sweeteners, such as

saccharin and aspartame have been introduced into the market gaining acceptance from the public consumer. Saccharin, which is approximately 300 times sweeter than sucrose, was discovered by Remsen and Fahlberg at John Hopkins University in 1879. Aspartame, better known by the trademark Nutrasweet, was discovered in 1965 by James Schlatter, a chemist with G. D. Searle and Company, while working on a new anti-ulcer drug. At present, other promising sweeteners, miraculin and monellin, are being studied for their potential use in the American market.

Finally, the induction of sweetness in foods is now being approached in a rather unique manner. The new method is termed molecular compartmentalization. By linking the sweetener to non-absorbable molecules, the metabolic hazards occurring after absorption are eliminated, and the taste benefits are obtained without risk.

C. Sucrose

The most commonly used sweetener is sucrose. Nonetheless, its consumption in the United States has decreased from 102 lbs per person in 1972 to 67.5 lbs per person in 1984 (Barry, 1984). This can be attributed to the increasing cost of sucrose in 1974 which prompted a search for a less expensive alternative. This

alternative was provided by the availability of HFCS with a 42 percent fructose content. In fact, the use of HFCS per capita has jumped from 0.7 lbs in 1970 to 36.3 lbs in 1984 (Barry, 1984). Regardless of a decrease in consumption, sucrose continues to be widely used by the Food Industry.

1. The Role of Sucrose in Foods

The various methods of use of sucrose are based on its physical and chemical properties (Koivisto and Hyvonen, 1985). In addition to sweetness, sucrose has several technological attributes that makes it desirable for the Food Industry. The most important among these are that sucrose in foods acts as:

- a. sweetener
- b. preservative
- c. flavor blender and modifier
- d. texture and bodying agent
- e. caramelization / color agent
- f. bulking agent
- g. fermentation substrate

The physical and chemical properties of sucrose also impose several limitations on its use in the food industry.

- a. The high concentrations (osmolarity) of sucrose

used in canning processes affect the visual appeal of the canned products- e.g. shrinkage and wrinkling of canned fruit.

- b. Sucrose is hygroscopic; therefore, it is difficult to freeze-dry food containing high concentrations of sucrose.
- c. It chars at high temperatures; therefore, sucrose can not be used to sweeten items that must be fried.
- d. Sucrose supports bacterial growth; therefore, bacterial contamination and spoilage of foods are possible.

2. Health Aspects of Sucrose

In 1958, Congress passed a Foods Additive Amendment that required preliminary marketing clearance and imposed regulations on the introduction of new products into foods (Ronk, 1978). Accordingly, all components added to processed foodstuff prior to 1958 were classified as food ingredients, whereas those added after were called food additives. With this act, the Congress authorized a list of food ingredients Generally Regarded As Safe (GRAS). Sucrose was listed as a food ingredient and placed on the GRAS list. Eventually, all items listed on the original list have come under review, sucrose being no exception.

The relationship of dietary sugar to health has been the subject of a number of reviews (FASEB, 1976; Stare, 1975; Grande, 1975; Danowski et al., 1975a; b; Bierman and Nelson, 1975; Finn and Glass, 1975). These reviews illustrate a large number of misconceptions regarding the relationship between dietary sugar consumption and health.

An evaluation of the safety of sucrose in food by the Select Committee on GRAS Substances of the Federation of American Societies for Experimental Biology concluded that the only toxic manifestation associated with sucrose was the formation of dental caries. Other than the contribution to dental caries, there was no clear evidence in the information available on sucrose demonstrating a hazard to the public when used at current level (FASEB).

A report published by the Sugars Task Force (1986), at the request of Dr. Sanford A. Miller, Director Center for Food Safety and Applied Nutrition, concluded that with respect to the general recognition of the safety of sugars contained in the food supply:

"The average daily intake for added sugars as a percentage of the daily calorie intake for the total population (11%) approximates the amount (10%) recommended by the Select Committee on Nutrition and Human Needs in its second edition of

Dietary Goals for the United States.

Evidence exists that sugars as they are consumed in the average American diet contribute to the development of dental caries.

Other than the contribution to dental caries, there is no conclusive evidence that demonstrates a hazard to the general public when the sugars are consumed at the levels that are now current and in the manner practiced".

From the above, it is quite clear that with the exception of dental caries (Alfano, 1980), there is no conclusive body of research to support direct cause-and-effect relationships between the use of sugar and obesity, cardiovascular disease, hypoglycemia, and diabetes in man (Leveille, 1980).

3. Role in Caries Formation

The most important caries-promoting component of food is the presence of the so-called 'fermentable' carbohydrates. Simple sugars are the most cariogenic of these compounds (Alfano, 1980). Bowen (1979) states that "the evidence incriminating sugar has continued to accumulate from the results of epidemiological and animal research and has now reached such proportions

that no reasonable person would deny that frequent consumption of sugars by caries susceptible humans will result in the development of dental caries". Extensive controlled human studies have contributed to the understanding of the relationship between sucrose consumption and its cariogenicity.

A study concluded by Orland et al. (1955) with rodents in a gnotobiotic (germ-free) environment demonstrated that bacteria are essential for caries development, regardless of the diet. The local action of the sugar in the mouth was demonstrated by Kite et al. (1950): rats fed a cariogenic diet by stomach-tube did not develop caries. Konig et al., (1968) showed a direct correlation between caries severity in rats and the frequency with which they were fed a cariogenic diet.

Animals studies have been supported, and further clarified by several human studies. The biggest single study in the field of dental caries ever undertaken is the Vipeholm Study (Gustaffson et al., 1954).

The Vipeholm Study was conducted at a mental institution in southern Sweden. Adults patients on an adequate diet were observed for several years and found to develop caries at a slow rate. Subsequently, the patients were divided into seven groups to compare the cariogenicity accompanying various changes in the frequency and consistency of their carbohydrate intake.

Sucrose was included in the diet as toffee, chocolate, caramel, in bread or in liquid form.

The main conclusions of the Vipeholm Study were summarized by the authors as follows:

"The risk of sugar increasing caries activity is great if the sugar is consumed in a form with a strong tendency to be retained on the surfaces of the teeth.

The risk of sugar increasing caries activity is greatest if the sugar is consumed between meals and in a form in which the tendency to be retained on the surfaces of the teeth is pronounced with a transiently high concentration of sugars on these surfaces.

Increase in caries activity due to the intake of sugar-rich foodstuffs consumed in a manner favoring caries disappears on withdrawal of such foodstuffs from the diet.

Cariou lesions may continue to appear despite the avoidance of refined sugar, maximum restriction of natural sugars and total dietary carbohydrates.

The risk of an increase in caries activity is intensified with an increase in the duration of sugar clearance from saliva".

A large number of studies illustrating the

relationship between sucrose and its cariogenicity has been publicized since the Vipeholm Study. Rugg-Gunn and Edgar (1983) have written an outstanding Review of Sugar and Dental Caries: The Evidence.

a. Ideal Substrate for Cariogenic Flora

Caries promoting carbohydrates are characterized by their ability to be rapidly metabolized by plaque microorganisms to produce organic acids (lactic, acetic, and propionic) in sufficient concentrations to lower the pH of plaque to levels resulting in some demineralization of enamel. Complex carbohydrates-e.g., starches, also can be hydrolyzed by salivary enzymes to release glucose, and subsequently be fermented by Streptococcus mutans promoting low level caries in laboratory animals (Thomson and Wills, 1976; Finn and Glass, 1975; Bibby, 1978); however, the role of dietary sugars as cariogenic substrates for dental plaque microorganisms is pre-eminent (Bowen, 1978).

Oral microorganisms metabolize most dietary sugars and fermentable carbohydrates in four basic ways (Alfano, 1980):

1. Bacteria synthesize adhesive bacterial extracellular polymers which assist the bacteria in sticking to the tooth and to each other, thus aiding in the colonization of the

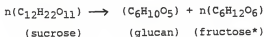
tooth.

2. Bacteria synthesize intracellular storage polysaccharides for use in cell metabolism when dietary substrate is not immediately available to the microorganism.
3. Bacteria synthesize extracellular storage polysaccharides.
4. Most importantly, bacteria use carbohydrates in the glycolytic pathway, resulting in the production of organic acids.

Most living cells are able to utilize monosaccharides, including the digestion products of sucrose, as a source of energy to fuel the glycolytic cycle for the synthesis of ATP. The production of organic acids by oral microorganisms during the glycolytic metabolism is thought to be directly responsible for the initiation of dental lesions. The synthesis of adhesive and storage polysaccharides facilitates the attachment of bacteria, especially of Streptococcus mutans to plaque, the long-term viability of the microflora and the perpetuation of the carious lesion. However, it is only from sucrose that most bacteria are able to synthesize both soluble and insoluble extracellular polymers (dextrans and mutans). Unlike other disaccharides, sucrose can also serve as a glycosyl donor in the synthesis of extracellular

polymers. The biosynthesis of both adhesive and storage polymers can be driven without other energy sources by the free energy of the hydrolysis of sucrose, and mediated by extracellular and membrane-bound enzymes with a high specificity for sucrose. The enzymes, the glucosyl- and fructosyl-transferases, have been isolated from Streptococcus sanguis and Streptococcus mutans, and have been characterized by Newbrun (1977) as follows:

1. They are highly specific for sucrose and will not utilize sugars such as fructose, glucose, maltose, or lactose.
2. They have a broad pH optimum, 5.2 - 7.0, coinciding with the pH range prevailing in dental plaque.
3. In the presence of adequate nutrition, the enzyme will be made by these microorganisms; sucrose is not a required inducer. Whenever sucrose is ingested, these microorganisms are ready to synthesize polysaccharides.
4. The equilibrium of the reaction shown below for glucan synthesis is far to the right.



* The fructose can be readily fermented by most plaque microorganisms to form organic acids.

The high specificity of these enzymes has led some researchers to regard sucrose as an unique substrate for cariogenic flora. Nonetheless, studies comparing the cariogenic activity of sucrose to other sugars have led to contradictory results depending on several factors.

The importance of sugar ingestion as a factor in the caries process has been explored by Konig et al. (1968). These studies clearly verified the conclusion of the Vipeholm Study in regard to the frequency of consumption of sucrose-containing foods in caries development. Frequent ingestion of sucrose (over 5 times per day), even at relatively low concentrations of 1.25 %, will cause a drop in pH to between 4 and 5 depending on the site and the method of measurement.

Susceptibility to dental caries has been also related to oral clearance times, and was clearly shown in the Vipeholm Study. Lundquist (1952) indicated that retentive, sticky, sweet foods with little detergency or self-cleaning properties may be potentially more cariogenic than foods that are detergent and clear rapidly from the oral cavity. Thus, the form of the fermentable carbohydrate dictates, to some extent, the length of contact-time between the sugar and the bacterial plaque. Sugars in liquid form, for instance, are rapidly cleared and less acidogenic than sugars mixed with retentive starches (Adorjan and Stack, 1976).

Contact time for plaque/substrate interaction can also be lengthened by increasing the frequency of carbohydrate ingestion (Edgar et al., 1975).

The concentration level of sucrose most detrimental from a caries standpoint is not simply decided. This relates to the availability of sucrose as substrate for bacterial organisms, which is influenced by the texture, consistency of the food, the stimulation of saliva elicited by chewing and the rapidity of clearance of the substrate. Nonetheless, Newbrun (1979) shows data tending to indicate that foods containing over 15 to 20 % sugar, especially sucrose, should be considered potentially cariogenic and unsafe as snack food.

A word of caution is necessary at this point.

Although research suggests that sucrose is more cariogenic than other sugars, the results are not all in agreement. This relationship between sucrose and caries exists only because sucrose is the sugar eaten most often and in greatest quantity. Thus, all common sugars are cariogenic; however, sucrose can, in some conditions be more so than other sugars.

III. ASPARTAME: A NON-CARIOGENIC SWEETENER

Dental caries (decay) is by far the most widespread disease in advanced societies throughout the World (Grenby, 1984). Since the development of dental caries depends upon the co-existence of several complex factors, it is not possible to prevent it totally by a single method (Ikeda, 1982). Over the years, many plans of actions have been suggested to protect the teeth against caries attack; however, the most fundamental approach is to improve the diet and our present-day eating habits in order to minimize the likelihood of their promoting caries. Furthermore, dental research has indicated that sugar substitution in a variety of foods ingested in modern society would be effective in reducing dental decay. In consequence, the desire for sweet foods and sweet drinks without their potential to cause dental caries has encouraged the development and use of sweeteners less cariogenic than sucrose. Thus, the burden of improving the diet has been taken away from the consumer and placed it on the hands of the manufacturers of confectionery, soft drinks, and other kinds of sugar-containing foods.

A. Sugar Substitutes: Reasons for their Use

1. Relative Sweetness

Sweetness is a subjective measurement which depends

Table 2. Relative sweetness of Alternative to Sucrose
(O'Brien and Gelardi, 1986).

Alternative sweetener	approximate sweetness (sucrose=1)
Acesulfame k	200
Aspartame	180
Chloroderivatives of sucrose	5 - 2000
Cyclamate	30
Dihydrochalcones	300 - 2000
Pure crystalline fructose	1.2 - 1.7
Glycyrrhizin	50 - 100
HFCS, 55 %	1
HFCS, 90 %	1.5
L- sugars	1
Mannitol	0.7
Monellin	1500 - 2000
Saccharin	300
Sorbitol	0.54 - 0.7
Steviose	300
Talin	2000 - 3000
Xylitol	1

HFCS = High Fructose Corn Syrup

on several factors, including the concentration of the sweetener, temperature, pH, type of medium used, and sensitivity of the taster. Sucrose is the usual standard and it is assigned a value of 1.0. Table 2 provides the relative sweetness of alternatives to sucrose made on a weight basis.

2. Purposes of Alternative Sweeteners

The search for sugar substitutes was originally initiated as a response to the needs of diabetic patients; however, alternatives to sucrose now serve many purposes, including among them the following (O'Brien and Gelardi, 1986).

- a. expand food and beverage choices for those who must or want to control caloric, carbohydrate, or specific sugar intake;
- b. assist weight control or reduction;
- c. aid the management of diabetes;
- d. possible reduction of dental caries;
- e. enhance the usability of pharmaceuticals and cosmetics;
- f. provide sweetness when sugar is not available (e.g., in various countries during WW I and WW II); and,
- g. assist the cost-effective use of limited resources.

Furthermore, alternative sweeteners can provide valuable properties other than sweetness, for example, texture, bulk, crystallization, and food preservation. Sweeteners are also stable in solid form and in solutions at wide ranges of temperature and pH (Rugg-Gunn and Edgar, 1987).

There is an expanding variety of sugar substitutes in the market, and each one of them exhibits a range of properties suiting them for a number of functions in foods. Bulk sweeteners (e.g., sorbitol, mannitol, xylitol, lycasin, and isomalt) provide bulk or 'body' in foods. Usually less sweet than the intense sweeteners, they are related to the carbohydrates. Intense sweeteners (e.g., saccharin, aspartame, and thaumatin) are also known as non-caloric or low-caloric sweeteners because most of them do not provide the body with any energy. Due to their high intensity of sweetness, they are used in minute amounts, blended with sugar and bulk sweeteners in solid foods, and replace sugar in soft drinks. Intense sweeteners are not related to carbohydrates.

Complete replacement of sucrose by alternative sweeteners is unlikely to occur, at least at this stage. No matter how attractive they are, sugar substitutes still lack many of the good qualities that make of sucrose such a valuable ingredient in the Food Industry.

Nonetheless, a reduction in sucrose consumption through total or partial replacement of the same in certain food products, shows potential for an improved dental health. In the other hand, the abundance of sweeteners in the market provides the consumer with alternatives to sucrose.

3. Non-Cariogenic Sweeteners

The dental professionals, of course, have become interested in non-cariogenic sweeteners. Table 3 summarizes the factors responsible for the cariogenicity of sucrose as a substrate.

Table 3. Main factors in the Cariogenicity of Sucrose as Substrate (Ikeda, 1982, p. 33).

Factor	Action
1. Formation of sticky insoluble glucan by <u>S. mutans</u>	Plaque formation, and interruption of acid neutralization by liquids in plaque etc.
2. Aggregation of certain plaque bacteria	Formation of cell cluster (precursor of plaque) on tooth surface
3. Acid formation	Deminerlization of tooth

It is understandable that for a sweetener to be regarded as non-cariogenic, it should have, in addition to suitable properties as a food ingredient, none of the listed characteristics.

Sugars and sweeteners differ in their effects on plaque and saliva. Sugars stimulate plaque glycolysis, flow of saliva, and a decrease in salivary pH. Sweeteners, although able to stimulate the flow of saliva and elevation of its pH, have small or no effect on bacterial glycolysis (Makinen and Virtanen, 1978). The plaque pH rises with sweeteners because the pH of saliva increases with increase in the flow rate and plaque bacteria produce base from the substrates provided by the saliva. Sweeteners will reduce prolonged periods of acid production, decreasing the chances of tooth demineralization and caries development. Figure 2 illustrates the role of nutritive and non-nutritive sweeteners in causing caries.

On the basis of the dental evidence, no overwhelming advantage can be attributed to any single bulk sweetener (Rugg-Gunn and Edgar, 1987). Sorbitol, for example, can be fermented slowly by oral bacteria (Guggenheim, 1968; Havenar et al., 1979; Drucker and Verran, 1979) and by plaque suspensions 'in vivo' (Hayes and Roberts, 1978; Birhead and Edwardson, 1979). There is also evidence that Streptococcus mutans adapts to

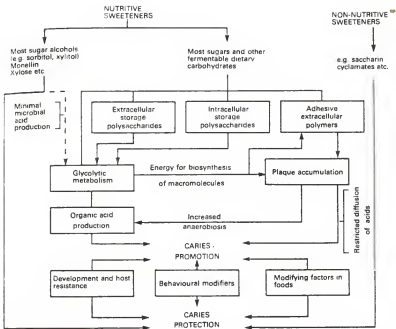


Figure 2. Role of Nutritive and Non-Nutritive Sweeteners in causing Caries (Alfano, 1980).

sorbitol substitution after prolonged usage (Scheinen and Makinen, 1975). In addition, a laxative effect results if sorbitol is eaten in quantity. Evidence of sorbitol non-cariogenic properties has been illustrated by its careful use in selected items, such as chewing gum (Finn and Jamieson, 1967; Moller and Poulsen, 1973; Banoczy et al., 1981).

In vitro studies have indicated that xylitol can be fermented slowly (if at all) to acid by oral microorganisms (Makinen, 1976; Hayes and Roberts, 1978; Druker and Verran, 1979). Xylitol produces less of a laxative effect than sorbitol or mannitol. The non-cariogenic properties of xylitol are explained by an increased rate in salivary flow, and an increase in salivary calcium concentration occurring when the xylitol material is chewed. Nonetheless, there are certain doubts concerning its carcinogenicity in rats (Ikeda, 1982). Slow absorption of xylitol from the intestinal tract has been shown to cause osmotic diarrhea. Health and safety aspects of xylitol are currently under FDA scrutiny.

Lycasin offers a better profile from the manufacturer's standpoint. It is non-cariogenic and lacks a laxative effect. However, Lycasin is about 25 % more expensive than sucrose.

Potential use of isomalt is limited by the little

, information available.

Most research has been directed to the investigation of the caries-inhibitory properties of intense sweeteners. Not related to carbohydrates, their composition make them unlikely fermentable substrate for oral bacterial. They are used in small concentrations; therefore, their indirect effects on caries are likely to be more important than direct inhibition on bacterial metabolism.

Saccharin inhibits bacterial growth and metabolism (Linke, 1977; Grenby and Bull, 1979; Brown et al., 1982), although little inhibitory effect was shown on rat caries development (Grenby, 1984). Thaumatin, a sweet tasting protein extracted from a plant found on West Africa, has been shown to favor remineralization of early caries in rats (Leach et al., 1983).

The use of aspartame, another intense sweetener, has increased rapidly over the years. Currently used in soft drinks, it also shows potential for use in many other food products, especially dried or frozen foods.

The following sections of this chapter are dedicated entirely to explore the properties of aspartame, and survey dental research related to this intense sweetener.

B. Aspartame: An Intense Sweetener

The sweet taste of the compound N-L- aspartyl-L-phenylalanine-1-methyl ester was discovered accidentally in December, 1965, by Mazur and Schlatter working at GD Searle (Mazur, 1976). Following the discovery, Searle spent two years investigating about 200 analogs of aspartame (APM), but decided to commercialize the original discovery, which became known by the generic name aspartame (Mazur et al., 1969). Among the major reasons for the choice of the original compound was the fact that aspartame is made of normal dietary components, L-aspartic acid and L-phenylalanine, and the body metabolizes them normally. This, observed Searle, gave aspartame excellent chances of surviving the most severe toxicity testing. Time proved Searle to be right, as APM became the most thoroughly studied food additive ever approved by the U.S. Food and Drug Administration, and a model for the clinical testing of a food additive (Stegink, 1987).

1. Physical Characteristics and Chemistry

Aspartame is a fine white crystalline powder having a sweet taste. It is slightly soluble in water (about 1 % at 25 C) and is sparingly soluble in alcohol (Beck, 1974). It is not soluble in fats and oils.

Being a peptide, the compound is amphoteric. The

negative log of its dissociation constants are 3.1 and 7.9 at 25 C, and its isoelectric point is 5.2 (Mazur and Ripper, 1979).

ASPARTAME

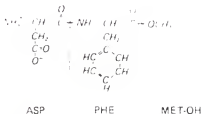


Figure 3. Chemical Structure of Aspartame (O'Brien and Gelardi, 1986).

The ester bond can be hydrolyzed in liquids and under certain conditions of moisture, temperature, and pH, forming the dipeptide aspartylphenylalanine and methanol. Eventually, methanol is eliminated by the cyclization of aspartame to form its diketopiperazine (DKP), and the dipeptide is hydrolyzed to its individual amino acids (Mazur and Ripper, 1979).

Dry aspartame is quite stable, and is affected only by extremely high temperatures (Beck, 1974). Moist storage and manufacturing conditions may produce the decomposition of aspartame. Figure 4 shows the principal conversion products of aspartame.

Aspartame is most stable between pH 3 and 5, with

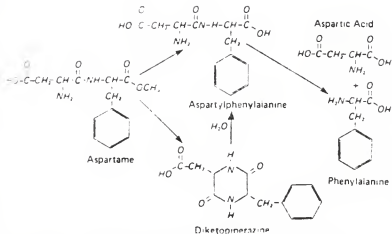


Figure 4. Principal conversion Products of Aspartame (O'Brien and Gelardi, 1986).

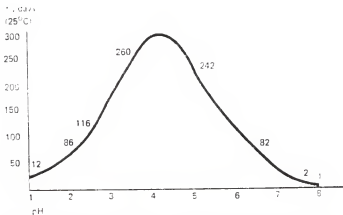


Figure 5. Stability of Aspartame in Aqueous Buffers at 25 C. (O'Brien and Gelardi, 1986).

Figure 5 shows the stability of aspartame in aqueous buffers at 25 C.

2. Food and Beverage Applications

Food and beverage systems can utilize aspartame in a variety of ways. Currently, aspartame is used as a sugar substitute in a number of products, such as breakfast cereals, toppings, mixes, frosting, chewing gum, dry mix beverages, and yogurt. Further use of aspartame has been extended to acidic foods, such as fruit juices and soft drinks, and as table top sweetener. In summary, aspartame can (Ripper et al., 1986; Waggoner, 1984) be used to:

- a. sweeten foods
- b. reduce calories as much as 95 %
- c. enhance flavors, particularly fruit flavors
- d. combine with sugars and artificial sweeteners
- e. reduce volume and weight of pre-sweetened products
- f. avoid nutrient dilution
- g. reduce viscosity, stickiness, or other properties associated with sugar
- h. reduce sucrose consumption

The sweetness potency of aspartame has been judged to be 160-220 times that of sucrose (Beck, 1974).

Because of its intense sweetness, only small amounts of aspartame are required for sweetening. Furthermore, the relative sweetness of aspartame varies with the flavor system, pH, tasting temperature, and the amount of sugar being replaced.

Aspartame is classified as a non-caloric, or low calorie intense sweetener. Thus, the amount of aspartame required to produce the sweetness effect equivalent to one teaspoon of sucrose produces only 0.1 Kcal, compared to 16 Kcal in one teaspoon of sugar.

Taste tests conducted by the manufacturer and university researchers indicate that aspartame has a sweet taste more like sucrose than any other substitute, and lacks the bitter aftertaste associated with other artificial sweeteners (Larson-Powers and Pangborn, 1978; McPherson et al., 1978).

Sensory evaluation studies give support to the flavor enhancement properties of aspartame. Naturally derived flavors, i.e. acid fruit flavors, are favored over artificial flavors; therefore, lesser amounts of aspartame are introduced into the products (Baldwin and Korschegen, 1979). Any lingering sweetness from aspartame can be modified with salts, or using slightly less sweetener.

Aspartame can not be used in all foods because its sweetness is lost at high temperature. It cannot be

used in alkaline foods either. The formation of diketopiperazine (DKP), which reduces its sweetness, limits aspartame applications in products to be baked or fried, or in processes calling for high temperature for extended periods of time (HTLT). However, some heat processing, for instance, high-temperature-short-time (HTST) pasteurization of dairy products, is possible if care is used. Frozen or refrigerated foods, on the other hand, show little change in aspartame content (Beck, 1978).

Aspartame loses sweetness when stored under less than ideal conditions, such as a combination of moisture, pH, and temperature, but without the development of off-flavors because the conversion products are tasteless. Nonetheless, sensory analyses tests have demonstrated a wide range over which aspartame sweetness levels are preferred to both saccharin-sweetened drinks and those sweetened with a blend of aspartame and saccharin (Beck, 1978; Searle and Co., 1982).

3. Safety Issues

In terms of total number of studies conducted before its approval, aspartame is one of the most thoroughly tested food additives (Stegink, 1987). It has been the subject of over 112 scientific studies

concerning metabolism, pharmacology, and toxicology (Hile, 1981; Matthews, 1984). All results indicate that the ingestion of aspartame at projected intake levels is no more hazardous than normal dietary consumption.

Aspartame is hydrolyzed in the gastrointestinal tract to its constituent amino acids, aspartic acid and phenylalanine, and to methanol. The body treats these compounds in a manner identical to that occurring when these components are found in ordinary daily food (Opperman et al., 1973a; 1973b, and Ranney et al., 1976).

Pharmacology studies were performed on all major physiological systems. All investigations demonstrated a total lack of pharmacological activity associated with aspartame (Brunner et al., 1979). No significant toxic or carcinogenic effects were attributed to aspartame consumption (Sturtevant, 1985; Ishii et al., 1981; Reno et al., 1975).

Teratology studies showed that dietary administration of aspartame has no significant effect on fertility, the development of fetal abnormalities or maternal survival (Lennon et al., 1980). The mutagenicity frequency was not altered, and no mutagenic activity was observed in any assay, 'in vivo' or 'in vitro', even after substantial doses of aspartame were fed over extended period of time.

Aspartame converts slowly into a diketopiperazine (DKP) under certain storage conditions. Therefore, in addition to the hydrolysis products: aspartic acid, phenylalanine, and methanol; aspartame may contain small amounts (less than 1 %) of diketopiperazine. Nonetheless, teratology, mutagenicity, toxicology, or pharmacology tests have shown no adverse effects directly attributable to DKP up to large doses of 3g/kg (Burgert et al., 1985).

The clinical trials and series of human studies with aspartame is unprecedented for a food additive prior to its approval (Hayes, 1981). After the Food and Drug Administration (FDA) set the acceptable daily intake (ADI) for aspartame at 50 mg/kg/per day, short term (6 weeks) and long term (12 weeks) clinical studies were conducted in order to demonstrate that aspartame is well tolerated by normal adults, children, and adolescents. The studies indicated no untoward effects, even at four times the recommended ADI, on normal human beings (Filer et al., 1983; Stegink et al., 1977).

Human studies were also conducted in special sub-groups of the population. Diabetic and obese populations were expected to consume larger amounts of aspartame-containing products because of their dietary requirements. Both diabetic and obese persons were found

to tolerate aspartame ingestion well, even at larger doses (Bauer-Nehrling et al., 1983; Knopp et al., 1976). No significant effects were noted on lactating women evaluated for the composition of their milk (Stegink et al., 1979).

Clinical studies were also conducted on individuals suffering from phenylketonuria (PKU). This is a genetic disorder that interferes with the phenylalanine metabolism and may lead to a progressive mental retardation unless the phenylalanine intake is limited strictly. The studies indicated that aspartame was metabolized in an identical manner to any other phenylalanine-containing product (Koch et al., 1976; Stegink et al., 1981). The phenylalanine from aspartame must be included in the daily calculations of PKU patient diets; therefore, FDA requires labeling, 'Phenylketonurics: contains phenylalanine', for all foods containing aspartame.

4. Worldwide Status

Aspartame has been approved for use in over 50 countries. The countries with the broadest approvals include the United Kingdom, Japan, the United States, South Africa, and Switzerland.

In addition to the USFDA, aspartame is also approved by the World Health Organization (WHO), the

European Economic Community (EEC), and other regulatory agencies around the World. The Council on Scientific Affairs of the American Medical Association (AMA) concluded that aspartame ingestion is not associated with serious adverse health effects (AMA Council on Scientific Affairs, 1985). The American Dental Association (ADA) has also issued a statement supporting the approval of aspartame (ADA, 1981).

C. Aspartame as an Aid to Dental Health

The intense sweeteners should be classified as non-cariogenic (Rugg-Gunn and Edgar, 1987). It has long been assumed that because of their non-carbohydrate structure, intense sweeteners do not promote tooth decay. Therefore, no further studies were deemed necessary. This has limited the amount of research undertaken on the non-cariogenic properties of aspartame (Grenby, 1984). In addition, most of the available data on aspartame are based on 'in vitro' experiments, and the results are conflicting at times.

Aspartame cannot be utilized as a fermentable substrate for Streptococcus mutans metabolism because it is a dipeptide. Since aspartame is not a carbohydrate, it is expected to reduce dental caries by limiting the amount or frequency of fermentable sugar in the diet. Furthermore, there is limited evidence that aspartame

may be capable of reducing caries by other means, and diet, of course, is one of several aspects involved in dental decay.

Another factor limiting the number of studies on the non-cariogenic properties of aspartame is the thought that aspartame is unlikely to completely replace sucrose due to its self-limiting properties as a food ingredient. Aspartame cannot be used for baking, nor can provide the bulk or browning capability of sugar in a recipe. In view of this, most studies have been conducted with aspartame in the presence of other sweeteners.

Linke and Chang (1976) studied the effects of aspartame and other sweeteners on various strains of Streptococcus mutans. They found that although aspartame alone could not sustain growth of the strains, when it was present in solution with glucose, aspartame did not affect the growth of Streptococcus mutans. No effects on the acid production of Streptococcus mutans during glucose fermentation were noted for aspartame.

Olson (1975, 1977) measured the adherence of Streptococcus mutans in the presence of different sweeteners. As expected, aspartame alone inhibited or retarded the formation of adherent plaque; however, in the tubes containing sucrose plus aspartame varying amounts of adherent plaque were obtained depending both

on the concentration of aspartame and sucrose. A combination of aspartame, saccharin, and cyclamate with sucrose, demonstrated that when aspartame was combined with sucrose, there was a significant decrease in adherent plaque. No effect of aspartame on acid production by bacteria was found in the study. Olson (1977) concluded that the reduction noted with aspartame indicates that peptides of aspartic acid (ASP) and phenylalanine (PHE) might be useful in the reduction of adherent plaque and warrants further work with peptides of this nature.

Concerned about the potential toxicity from the hydrolysis products of aspartame, Longton and Cole (1976) conducted a study focused on the interaction of human oral fluids with aspartame, and the potential for oral tissue toxicity from aspartic acid, a breakdown product as found in the gastrointestinal tract. Aspartame was partially broken on incubation with saliva. The measurable levels of aspartame were reduced by 50 % in 30 minutes of exposure to whole saliva and by 90 % in a similar exposure to parotid fluids. The products formed from these reactions with saliva were not identical to the expected gastrointestinal products cited above.

Mishiro and Kaneko (1977) examined the acid production of plaque in glucose and aspartame mixtures

in the presence of human whole saliva. Aspartame seemed to have two kinds of effects: (1) increasing the pH of the aspartame and glucose mixture; and (2) inhibiting a fall in pH of the mixture of aspartame and glucose equal to the fall seen with glucose alone. Similar observations were obtained when aspartame constituent amino acids were used individually, and not so with an amino acid solution. The effect of chewing gum on resting plaque pH was investigated by Soparkar et al. (1978). Two commercially available sugarless gums, and a gum containing sorbitol, mannitol, and aspartame produced an increase in pH differing markedly from the depression of plaque pH produced by a chewing gum containing sucrose. It was seen that the sugarless and aspartame gums raised rapidly the depressed pH of the dental plaque previously treated with sucrose above the initial level and recovered to that level, while the sugar gum increased the plaque pH slightly but it quickly returned to levels below the initial level. How much of this is due to aspartame is hard to answer since other sweeteners, in addition to aspartame, were utilized in the experiment.

The effect of aspartame on dental caries was examined in a study conducted by Reussner and Galimidi (1981). They compare the effects of adding aspartame or saccharin to a modified basal cariogenic diet (BCD)

containing a mixture of carbohydrates resembling the components of the American diet. Laboratory rats were inoculated with Streptococcus mutans and fed the BCD with and without 0.25 % and 0.5 % of each synthetic sweetener for 60 days. Saccharin gave a dose related significant decrease in occlusal caries, but no decreases in buccal dentinal caries. Aspartame resulted in a non-significant dose related decrease in buccal dentinal caries and non-significant decreases in occlusal dentinal caries. The researchers concluded that saccharin and aspartame differ in their caries inhibitory effects on occlusal and buccal tooth surfaces. These findings are in agreement with those reported by Tanzer and Slee (1983).

Previous claims that aspartame could offer some protection against tooth enamel remineralization (TED) were investigated by Reussner et al.(1982). Their study examined the effects of aspartame on tooth enamel remineralization in laboratory rats resulting from a 0.2 % citric acid solution. When aspartame replaced a 10 % sucrose solution at an equivalent level (0.58g/L) there was a significant decrease in TED from 3.46 to 2.65 ($p < 0.05$). On the other hand, the replacement of aspartame with saccharin at an equal sweetness level did not reduce the TED score when compared to the sucrose control. Furthermore, the same level of aspartame

significantly enhanced the effects of monocalcium phosphate for preventing tooth enamel remineralization.

Grenby and Saldanha (1983) compared aspartame with other nitrogenous substances as a nitrogen source for acidogenic oral microorganisms. A standard mixed saliva culture was inoculated into a basal nitrogen-free liquid growth medium containing set concentrations of aspartame, ammonium sulfate, L-aspartic acid, other amino acids, or bovine albumin. After incubation at 37 C for 24 hour, turbidity, cell protein, pH and titratable acid were measured. Microbial growth and acid production were generally greatest when the medium contained ammonium sulfate, L-aspartic acid or mixtures of amino acids. These values were significantly lower when the sole source of nitrogen was aspartame, L-phenylalanine, or bovine albumin. Thus, in spite of the fact that aspartame promotes lactic acid production in saliva, these results indicated that it was poorly utilized by acidogenic oral microorganisms as a nitrogen source compared with other amino acids and nitrogenous compounds.

In 1986, Grenby and Saldanha studied the effects of five different intense sweeteners on the growth and metabolism of mixed cultures of dental plaque microorganisms or a pure culture of Streptococcus mutans NTTC 10449. The study was conducted in (a) a

peptone liquid media, (b) in agar media by the zone inhibition method, and (c) in tryptone soya medium by a modification of the minimum inhibitory concentration method. Acesulfam-K and cyclamate were found to have no anti-microbial activity. The effects from Talin were obscured by its tendency to precipitate from solution. Only aspartame and saccharin had any inhibitory action, with aspartame more effective in mixed plaque cultures and saccharin more effective against Streptococcus mutans. These results indicate a modest but distinct difference in the non-cariogenic properties of intense sweeteners and their effects on oral microorganisms.

A summary of the findings of dental research involving aspartame is presented in Table 4.

Contradictory results point toward the need of further studies on the effects of aspartame on dental health.

Table 4. Summary of Findings of Sweetening Agents
Compared to Sucrose (Waggoner, 1984).

Effect on Growth of S. mutans

Aspartame alone does not sustain S. mutans growth.
Aspartame with glucose yields normal S. mutans growth.
Aspartame alone forms no adherent plaque.
Aspartame with sucrose yields a decrease in adherent plaque.

Effect on Acid Production and Plaque pH

Aspartame with glucose shows acid production equal to glucose alone.
Aspartame with glucose shows an increase in acid production but an inhibited fall in pH.
Aspartame with sucrose shows acid production equal to sucrose alone.
Aspartame with sorbitol and mannitol produces and maintains an increase in plaque pH which has been depressed with a sucrose rinse.

Effect on Enamel Demineralization and caries

Aspartame reduces the amount of acid-induced enamel demineralization compared to a sucrose control.
Aspartame added to the diet of laboratory rats fed a basal cariogenic diet produces no significant changes in caries.

Aspartame is poorly utilized by acidogenic microorganisms as a nitrogen source compared with other amino acids and nitrogenous compounds (Grenby and Saldahna, 1983).

Aspartame shows inhibitory action on the growth and metabolism of mixed cultures of dental plaque (Grenby and Saldahna, 1986).

CONCLUSIONS

1. Dental caries, a transmissible and infectious disease caused by oral bacteria, is by far the most widespread disease in advanced societies around the World.
2. Animal research and controlled human studies indicate the fermentable carbohydrates, simple sugars, as the most important caries-promoting component of food.
3. Although all common sugars are cariogenic, sucrose can, in some conditions, be more so than other sugars.
4. Complete or partial replacement of sucrose in certain products by alternative substitutes shows potential for improved dental health.
5. Aspartame, a non-caloric intense sweetener, does not promote tooth decay; however, most data available on the non-cariogenic properties of aspartame are based on 'in vitro' experiments, and the results are conflicting at times.
6. The use of aspartame in foods is limited by its physical and chemical properties; however, replacement of aspartame for sucrose in certain food products may contribute to reduced tooth decay by decreasing the consumption of more cariogenic sugars.
7. Aspartame provides the consumer with an alternative

to sucrose.

8. Further clinical studies on the non-cariogenic properties of aspartame, as well as further uses of aspartame in food products, are to be encouraged.

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A RATIONALE FOR THE USE OF ASPARTAME AS A SUGAR
SUBSTITUTE IN THE POSSIBLE REDUCTION OF DENTAL CARIES

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ABSTRACT

According to the epidemiological model, dental caries (dental decay) results from the interaction between three primary factors (tooth, bacteria, and substrate), and secondary factors (saliva, oral hygiene, and diet). The experimental evidence in support of oral bacteria and a suitable local substrate as prerequisites for dental caries is overwhelming. Although there is discrepancy as to how and which microorganisms produce carious lesions, it is generally accepted that caries cannot occur without bacteria. Consequently, dental decay have been demonstrated to be a transmissible and infectious disease caused by oral bacteria.

The evidence incriminating the fermentable carbohydrates- simple sugars- as the most important caries-promoting component of food have accumulated from the results of epidemiological studies and animal research making possible the understanding of the relationship between sucrose consumption and its cariogenicity. Oral microorganisms are able to metabolize most dietary sugars and fermentable carbohydrates to produce organic acids in sufficient concentrations as to initiate the process of tooth demineralization. Evidence suggest that although all common sugars are cariogenic, sucrose can, in some conditions, be more so than other sugars.

In spite of the essential role of sucrose in foods, the search for sugar substitutes was initiated long time ago. Initially as a response to the needs of diabetic patients, alternative sweeteners now serve many purposes. Dental research have indicated that sucrose substitution in a variety of foods ingested in modern society would be effective in reducing dental decay. This report describes the rationale for the use of aspartame, an intense sweetener, in the prevention of tooth decay.

The conclusions of this report indicate that aspartame does not promote tooth decay; however, most of the data available on its non-cariogenic properties are based on 'in vitro' experiments, and the results are conflicting at times. Although complete replacement of sucrose by aspartame is unlikely to occur due to its limited chemical and physical properties, the use of aspartame in certain food products may contribute to promote dental health by reducing the consumption of more cariogenic sugars. In addition, aspartame provides the consumer with alternatives to sucrose. Further clinical studies on the non-cariogenic properties of aspartame, as well as potential applications of this intense sweetener in food products, are to be encouraged.