ALTERNATIVE SWEETENERS

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Lyn O'Brien Nabors
Robert C. Gelardi
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L-Sugars: Lev-O-Cal™

Gilbert V. Levin
Biospherics Incorporated
Rockville, Maryland

INTRODUCTION

The L-sugars comprising Lev-O-Cal are 6-carbon simple sugars (hexose monosaccharides). They are L-sugars by virtue of having left-handed molecular configurations at asymmetric carbon atoms.

On April 14, 1981, U. S. Patent No. 4,262,032 (1) for use of the L-sugars, L-glucose, L-allose, L-fructose, L-gulose, L-galactose, L-altrose, L-idose, L-talose, L-tagatose, or L-psicose, as low-calorie sweeteners in foods, beverages, and drugs was awarded and assigned to Biospherics Inc. Corresponding patients in a number of foreign countries, where obesity or sugar-related disease is a significant problem, have also been filed.

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BACKGROUND

The natural occurrence of L-sugars is rare, although they have been variously reported as minor unquantitated constituents in natural products:

- L-Galactose—flax seed gum; red algae; snail eggs
- L-Fructose—plantain seeds
- L-Rhamnose—plantain seeds
- L-Arabinose—araban (a polysaccharide) in sugar beets; mesquite, pectins, other plants
- L-Sorbose—berries from the mountain ash; other plants
- L-Fucose—seaweed

Until recently, L-sugars used in research were prepared from chemically synthesized sugars, a process that results in equal amounts of L and D forms (2-13). When the L/D mixtures were fed to bacteria, the D form was consumed, but the L form was left intact. Despite this easily demonstrated biochemical difference, with its indication that L-sugars might be noncaloric, apparently no one thought to use them as sweeteners. This was probably because of their scarcity and, also, the likelihood that they would not taste sweet. However, L-sugars have long been used as chemical markers or metabolic blocks.

The structural aspect of importance in L-sugars can best be described by beginning with the carbon atom, generally represented at the center of a tetrahedron with four bonding arms, each extending outward from the center to the four points (Fig. 1). Numerous other atoms or groups of atoms can bond with the carbon atom (Fig. 2). Considering two carbon atoms side by side, each bonding with an atom "A" at all four of its bonding sites, it can be seen the resulting structures are identical (Fig. 3). If each carbon atom bonds with three A's and a B in the manner shown in Fig. 4, they may, at first glance, appear to differ. However, by rotating one of the carbon atoms, the molecules can be superimposed and become identical (Fig. 5). The same identity prevails if the carbon atoms form four bonds with four groups of three different types (e.g., ABCA, ABCB, or ABCC) regardless of which bonds are made with which types. However, if all four bonded groups are different (ABCD), then the configuration cannot be

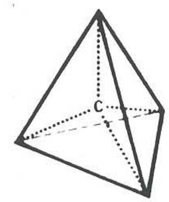


Figure 1

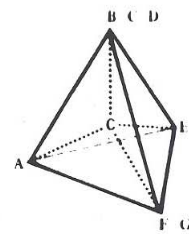


Figure 2

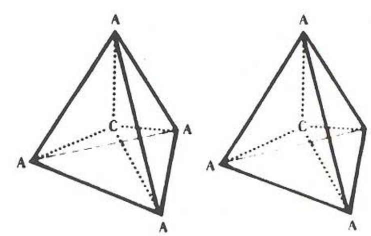


Figure 3

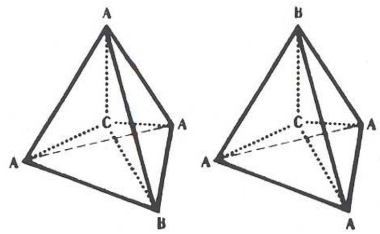


Figure 4

rotated into superposition (Fig. 6). If these groups are rotated to place any two of the bonds in identical positions, the remaining two will be reversed. These configurations are thus mirror images of each other, just as are our two hands, and so these compounds have come to be called "left-handed" and "right-handed" sugars. According to the universally accepted system of nomenclature, the configurations are termed "levo" and "dextro" and abbreviated L- and D- (the letters are distinct from the lowercase prefixes l- and d-, or the symbols + and −, used to indicate the direction of rotation of polarized light passing through a sugar solution).

The asymmetric carbon structures in fructose, i.e., dextro-fructose (or D-fructose) and levo-fructose (or L-fructose), are shown in Fig. 7. Having the same constituents, mirror-image molecules behave almost identically in chemical reactions. However, in the realm of biochemistry, this similarity may not hold true. In biochemistry, enzymes play an essential role by prompt-

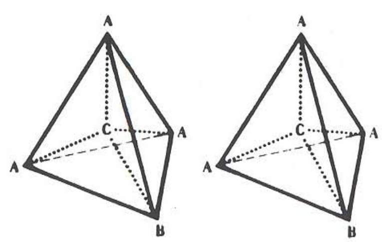


Figure 5

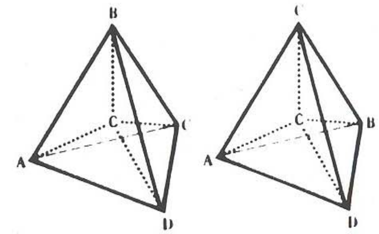
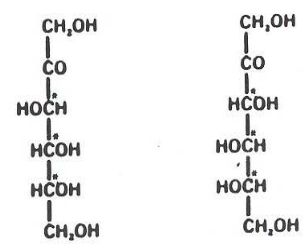


Figure 6

ing reactions that would otherwise not occur. This role requires that the enzymes physically fit the shapes of the reacting chemicals in order to bring them together for the reaction to take place. Hence, left-handed (L) sugars cannot fit the enzymes required for sugar metabolism (14) and, extrapolated to humans, should not give us their calories. This difference in caloric availability has been recognized since the time of Pasteur, and more recent findings (15) have supported the nonmetabolizable character of L-sugars.

CHEMICAL AND PHYSICAL PROPERTIES

Differing only because of their mirror relationship, the L and D forms of a particular sugar have identical chemical and physical



D-Fructose L-Fructose * Optically active carbon atom

Figure 7

characteristics, such as boiling points, melting points, solubilities, viscosities, textures, hygroscopicities, densities, colors, and appearances. Therefore, L-sugars are expected to yield similar food products when substituted for D-sugars, without the increased calories.

In tests comparing L-sugars with "regular" sugars, taste panels have now confirmed that the tastes of pure L-sugars are, within experimental error, the same as each of their respective D-sugar isomers (16). In comparison with other low-calorie sweeteners, L-sugars are superior in several important ways. They are as stable in aqueous solution as are their D-sugar counterparts. Among low-calorie sweeteners presently available, none are known to brown upon baking. L-Sugars are expected to look, handle, and perform in the same way as "regular" sugar.

Based on the foregoing, L-sugars should be:

1. Noncaloric for humans
2. Identical in taste to D-sugars
3. Noncariogenic because microorganisms in the mouth should not be able to produce tooth-decaying acids from L-sugars
4. Immune to spoilage or decay caused by common bacteria
5. A 1-1 substitute for D-sugars, requiring no bulking agent
6. Stable in aqueous solution
7. Stable in food processing including heating
8. Useful in baked products
9. Suitable for use by diabetics and sufferers of other sugar-related diseases

Theory, supported by limited biological experiments reported in the literature, predicts that L-sugars should provide a uniquely useful sweetener (17-24). However, functionality and safety must yet be established to FDA standards. Problems of functionality involve questions of whether there might be enzymes in the body that could be induced to transport L-sugar across the intestinal membrane and/or convert it to a metabolizable D-form; or whether microorganisms in the intestinal tract might metabolize the L-sugar to produce by-products which, in turn, could be utilized by the body. Safety questions run the gamut from acute toxicity through possible chronic and genetic effects. For example, reported experience with other sweeteners shows that some have a laxative effect.

SYNTHESIS

In addition to natural occurrence, L-sugars can be produced synthetically. Procedures now used are mostly chemical methods involving isomerization (conversion of a D-form into an L-form) and addition processes. Some enzymatic methods exist (25), and genetic engineering methods may be possible. The only L-sugar produced commercially at the present time is L-sorbose, prepared for use in manufacturing vitamin C (26).

MARKETING

Pending FDA approval, a program to develop L-sugar products will be initiated. The technology for one such product, L-gulono-γ-lactone, utilizes starch or cellulose as the starting material. Glucurone is produced and, in turn, is converted into L-gulono-γ-lactone through high-pressure hydrogenation. Finally, the lactone is transformed into L-gulose, one of the L-sugars. This product might then be marketed and, according to a 1978 analysis (27), L-gulono-γ-lactone can be produced at 89 cents per pound. Even at today's costs, and with the added step to make L-sugar, current estimates indicate production of L-sugar for less than $1.00 per pound. Considering that very early estimates went as high as $3000 per pound, this constitutes a major cost reduction and indicates commercial practicality. In addition, a program is underway to develop economical methods for the production of L-fructose.

STATUS

Toxicity testing must be completed prior to L-sugar approval for food products. At that time, primary application for L-sugar use could include chewing gum, candy, prepared foods (e.g., baked goods), and pharmaceuticals. Application for soft drink use would follow should test results warrant.

Manufacturing processes and production techniques for L-sugars are under development (28). These studies have the dual intent of obtaining test quantities of high-purity samples, as well as developing economical methods for industrial production. At present, approval for L-sugar is not expected before 1988.

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