A decade ago, a nearly 90 min long YouTube video by a California endocrinologist changed the way millions of people view the role of sugar in their diets. Its unlikely star, Robert Lustig, used his time in “Sugar: The Bitter Truth” to outline evidence for his contention that overconsumption of added sugars leads to chronic metabolic diseases.

The idea that, beyond their ability to inflate the calories of food, added sugars are uniquely bad for us is still controversial, but the circumstantial evidence is strong. Research shows that the consumption of added sugars is associated with the development of metabolic syndrome, which can lead to cardiovascular disease and type 2 diabetes.

Public health groups have taken up the cause and pushed for laws and rules they believe will reduce the ready availability of food high in added sugars. Sugar-sweetened sodas were first in the cross-hairs. Fourteen countries around the world now tax the drinks. In the US, taxes on sugary drinks can be found in only a handful of cities and counties. But a new national food-labeling policy will, for the first time, call out the amount of sugar added to packaged food and drinks. It will shine a harsh spotlight on the common food industry practice of adding sugar to almost everything on grocery store shelves.

Shoppers will soon see changes in the ingredients of the food and drinks they buy. To avoid cringe-worthy labels, food companies are trying to lower sugar levels without using the synthetic sweeteners that consumers have come to distrust. They are turning to a new arsenal of label-friendly sweeteners from ingredient suppliers using industrial biotechnology. Instead of the usual sugars, syrups, and aspartame, many of tomorrow’s labels will boast stevia molecules, the sugar alcohol erythritol, and a
Food firms test their options

Packaged-food firms see the new label requirement as a call to action rather than a reason to panic, industry experts tell C&EN. Most brands have been fielding requests from consumers to reduce added sugars for years. Moreover, the FDA first proposed the new label in 2014, meaning companies have had time to develop and test new formulations to avoid being called out for high sugar levels.

The most common reformulation to reduce added sugars involves swapping out a portion of sugar for no- or low-calorie sweeteners, according to market research. But other food trends are cutting into the palette of easy alternatives. For example, a majority of consumers say they avoid synthetic sweeteners and other artificial flavors. They are looking for foods with short, easy-to-comprehend lists of natural-seeming ingredients.

The prospect of difficult recipe changes opens up vast competitive space for ingredient companies. Firms including Cargill, Ingredion, and Tate & Lyle are offering new ways to reduce sugar that also meet consumer expectations for taste, appearance, texture, and cost. Their expertise has busted out of the healthy food category and is now needed everywhere.

“Food companies will make changes across most of their brands, not just in a specific area,” Yates says. “How much sugar they try to carve out depends on the consumer they are targeting, but I think even in indulgent items there is absolutely a focus to remove some percentage of sugar content.”

Food makers routinely work with their ingredient suppliers to strategize and test new recipes. Those efforts are multiplying as the pressure to reduce sugar moves beyond beverages into categories such as baked goods, dairy products, and even candy. Companies are moving ahead with confidence that lower-sugar products will become the norm.

“The larger issue is the demonization of sugar,” says Tom Vierhile, vice president of strategic insights for North America for the market research firm Innova Market Insights. “It continues, and I don’t think it will go away.”

Innova highlighted sugar-reduction strategies in June at the Institute of Food Technologists conference, a huge gathering of food scientists and companies. The firm presented data showing that 8% of all new food and beverage launches in the US featured a sugar-reduction claim, an increase of 55% from 2014, when the FDA announced the upcoming label change.

Of the new products with no-added-sugar, low-sugar, or sugar-free claims, 23% were in the soft-drink category. A similar number of introductions were in the sports nutrition group, showing how the trend toward ketogenic and other high-protein, low-carbohydrate diets helps fuel consumer demand for reduced- or no-sugar options.

Counting sugar claims on labels does not capture every case of sugar reduction, Vierhile points out. “You are seeing companies reduce sugar content in some cases in ways that are covert. They may not tell the consumer they are gradually whacking away to reduce sugar content. That will continue with the new labeling.”

Food companies don’t always wish to draw attention to their new recipes. For one thing, they are likely to phase in adjustments over time and don’t yet know how much reduction they will achieve. They may rely, at least in the near term, on artificial sweeteners, which are unpopular with three in five US consumers, according to Innova’s consumer survey data.

Those concerns may be why brands are not interested in talking publicly about their strategies. Kraft Heinz, Mondelēz International, and Nestlé declined to speak with C&EN about what they are doing to reduce sugar across their hundreds of food brands.

The pressure to reduce sugar levels will buoy zero- or low-calorie sweeteners, including synthetic alternatives, according to Yates. For example, sucralose, at 600 times the sweetness of sugar, will be an inexpensive go-to solution for many products. Brands that sell at a price point too low to accommodate expensive natural alternatives like stevia will continue to rely on synthetic sweeteners.

For diet beverages and reduced-calorie yogurt, the sugar-fighting duo aspartame and acesulfame potassium is a common choice. The combo has helped soda makers in the UK reduce sugar in nondiet sodas just enough to skirt the country’s sugar tax. Still, experts tell C&EN that most
Choosing sweeteners
The type of food or beverage, as well as customer preferences, dictates the best route to sweetness.

**Sucrose (table sugar)**
- Calories per gram: 4
- Cost: $0.68 per kilogram
- Natural

**Sucralose**
- Calories per gram: 0
- Sweetness compared with sugar: 600 times as sweet
- Cost: $50–$80 per kilogram
- Synthetic

**Rebaudioside M**
- Calories per gram: 0
- Sweetness compared with sugar: 208 times as sweet
- Cost: $440 per kilogram
- Natural

**Acesulfame potassium (Ace-K)**
- Calories per gram: 0
- Sweetness compared with sugar: 200 times as sweet
- Cost: $5–$10 per kilogram
- Synthetic

**Sucralose**
- Calories per gram: 0
- Sweetness compared with sugar: 600 times as sweet
- Cost: $50–$80 per kilogram
- Synthetic

**Erythritol**
- Calories per gram: 0.24
- Sweetness compared with sugar: 70% as sweet
- Cost: $8 per kilogram
- Natural

**Rebaudioside M**
- Calories per gram: 0
- Sweetness compared with sugar: 208 times as sweet
- Cost: $440 per kilogram
- Natural

**Allulose**
- Calories per gram: 0.4
- Sweetness compared with sugar: 70% as sweet
- Cost: $7 per kilogram
- Natural

**Sources:** Companies, US Food and Drug Administration, C&EN estimates.
brings hope to avoid using aspartame in new products, as many consumers erroneously believe it is unsafe.

**Market grows for naturals**

In coming years, stevia and its sweet-tasting glycosides are likely to make significant inroads into mass-market beverages thanks to innovations in plant breeding, enzyme technology, and organism engineering. Until recently, stevia sweeteners primarily contained rebauonolide A, the most abundant sweet molecule in the leaf of the stevia plant. But Reb A has a bitter, licorice aftertaste that can be hard to cover up, limiting widespread use of the natural sweetener.

Now, stevia-specialist firms PureCircle and SweeGen say they are close to being able to produce huge quantities of the rare glycoside Reb M, which tastes more like sugar. PureCircle spent years breeding its stevia plant to produce more Reb M. Last year the company said it was “massively ramping up” planting of the patented variety, called Starleaf.

Anticipating skyrocketing demand for Reb M, PureCircle has also figured out how to transform Reb A into the sweeter Reb M using an enzyme. The company explains that the process is similar to the cascade of enzymatic transformations that happen in the stevia plant to turn a portion of Reb A into other steviol glycosides.

SweeGen, a major supplier of stevia to Ingredion, also says it can make Reb M and any other targeted steviol glycoside with its own enzymatic process. It licensed enzyme strains and scale-up technology from the Boston-area biotech firm Conagen.

Both stevia firms are aggressively building out manufacturing capacity. SweeGen, aided by a new investment from Sumitomo Chemical, says it will expand its European manufacturing to produce 3,000 metric tons per year of stevia sweetener. PureCircle, meanwhile, says that within 3 years it will produce enough Reb M for 1 billion cases of zero-calorie soft drinks.

Cargill, which launched its plant-based Truvia sweetener in 2008, has additionally invested in a route to glycosides that doesn’t start with the stevia plant at all. It worked with the biotech firm Evolva to commercialize a process for making Reb M and sister molecule Reb D from sugar via fermentation with a modified microbe. After 6 years of R&D, Cargill started up production of its EverSweet stevia in March 2018.

As stevia sweeteners improve in taste and become cheaper, more applications are opening up. “We’ve had great success in a wide range of beverages, from chocolate milk and ready-to-drink sweet teas to plant-based protein drinks and low-calorie carbonated beverages,” says Vince Cavallini, Cargill’s application manager for beverage, dairy, and convenience foods.

But using stevia requires both expertise and tinkering. Like synthetic high-intensity sweeteners, stevia generally can’t replace sugar on its own. Compared with sugar, stevia is like a bad party guest. Its sweetness arrives fashionably late and sticks around long after more polite guests have gone home.

“We blend for early onset of sweetness and the right level of sweet taste all the way through,” says Scott Schultz, vice president of sales at Sweetener Solutions, which supplies premixed powdered sweeteners primarily to regional food and beverage firms.

The need for blends means stevia’s growing success will improve the fortunes of the sugar alcohol erythritol, as the two are often used together. Erythritol is only 70% as sweet as sugar, but it fixes a number of stevia problems: it adds a thicker mouthfeel to diet beverages, eliminates off tastes, and corrects stevia’s sweetness timing problem.

Not only that, but the two sweeteners are sweater together than individually. Pound for pound, stevia is sweeter than sugar, but there is a limit to how sweet a beverage can get with stevia only. On a scale called the sugar equivalent value, stevia scores an 8, but colas and diet teas require 10–12. “By blending stevia with erythritol, we get more up-front sweetness, enabling deeper sugar reductions,” Cavallini says.

The right blend of sweeteners can replace 50% or more of sugar without a noticeable change in taste, Schultz says. Once clients test such a recipe with consumers and no one notices the difference, he says, they often come back to take the next step to replace 75% or even 100% of the sugar.

Stevia is starting to expand beyond beverages into bakery, dairy, and frozen-dessert products, where further challenges await. In those foods, sugar provides much more than sweet taste. For example, in ice cream, sugar adds bulk and lowers the freezing point to minimize the formation of ice crystals and provide a smooth texture.

“In many ways, replacing sugar’s sweet taste is one of the easiest obstacles to overcome,” says Christine Addington, a senior dairy technical service specialist at Cargill. Stevia-based ice-cream recipes have to result in a soft, scoopable ice cream, not an icy mass. So food companies partner stevia with erythritol as in beverages, but they also call on an old-time food ingredient—chicory root fiber—for added bulk. Even then, ice-cream makers need to adjust stabilizers and emulsifiers to prevent water from migrating out of the matrix, Addington says.

Bakers can also incorporate similar stevia-erythritol-fiber combinations to reduce sugar by 15–20% in cookies and up to 50% in cakes and muffins.

**Anticipating a new solution**

Some bakers and ice-cream makers are holding out for a new, natural sweetener that promises all the sweetness and utility of regular sugar with few health or formulation downsides. It’s a sugar called allulose, and it exists naturally in figs and raisins. Its entrance to the market has been heralded by furious patent activity reminiscent of the innovation boom that resulted in today’s abundant stevia choices.

Allulose was discovered in the 1940s in the leaves of wheat plants and later in fruit, says Abigail Storms, vice president of sweetener platform innovation at Tate

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**Nutrition Facts**

<table>
<thead>
<tr>
<th>1 Serving Per Container</th>
<th>1 Bottle</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Calories</strong></td>
<td>240</td>
</tr>
<tr>
<td><strong>Total Fat</strong></td>
<td>0g</td>
</tr>
<tr>
<td><strong>Sodium</strong></td>
<td>75mg</td>
</tr>
<tr>
<td><strong>Total Carbohydrate</strong></td>
<td>66g</td>
</tr>
<tr>
<td><strong>Total Sugars</strong></td>
<td>65g</td>
</tr>
<tr>
<td><strong>Includes 65g Added Sugars</strong></td>
<td>130%</td>
</tr>
<tr>
<td><strong>Cholesterol</strong></td>
<td>0mg</td>
</tr>
<tr>
<td><strong>Protein</strong></td>
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</tr>
<tr>
<td><strong>Vitamin D</strong></td>
<td>0%</td>
</tr>
<tr>
<td><strong>Calcium</strong></td>
<td>0%</td>
</tr>
<tr>
<td><strong>Iron</strong></td>
<td>0%</td>
</tr>
<tr>
<td><strong>Potassium</strong></td>
<td>0%</td>
</tr>
</tbody>
</table>

Not a significant source of saturated fat, trans fat, cholesterol, dietary fiber, vitamin D, calcium, iron and potassium.

**Several sugar-sweetened sodas are already sporting the new Nutrition Facts label. A 20 oz (about 591 mL) bottle of Coca-Cola contains 65 g of added sugars, more than a day’s recommended allowance for an adult male.**
Few options to thwart a sweet tooth

Switching to no-calorie sweeteners doesn’t fix cravings, but a modern take on an ancient remedy might help

If you’ve vowed to cut back on sugar, you are in good company. A survey of US consumers by the research firm Label Insight found 47% planned to eat less sugar or buy more no-sugar-added foods in 2018.

Many people struggle to cut down on sugar. A study of adults diagnosed with metabolic syndrome who were coached for a year to reduce sugar in their diets showed the majority continued to exceed recommended limits for added sugar (Eur. J. Nutr. 2017, DOI: 10.1007/s00394-017-1390-6).

The World Health Organization says added sugars should account for no more than 10% of total calories consumed in a day, or a maximum of 50 g for an adult male on a 2,000-calorie diet. Ideally, we’d eat half that. Yet the average American consumes over 71 g, according to the US Department of Health and Human Services.

Clearly, health warnings alone will not fix our craving for sugar.

It’s hard to ignore those cravings in the face of cheap and tasty food with high levels of added sugars. But another factor is biology: the taste of sugar kicks off a cascade in our bodies that triggers the reward pathways in the brain’s limbic region.

Dieters may turn to foods sweetened with no- or low-calorie sweeteners like sucralose. But biology conspires against us again. Research shows that consuming the sweeteners does not reduce cravings or appetite (Curr. Gastroenteral. Rep. 2015, DOI: 10.1007/s11894-014-0423-7).

“Sucralose tastes sweet, but it doesn’t deliver what sweetness is promising—namely, calories,” says Gary K. Beauchamp, the emeritus director of the non-profit Monell Chemical Senses Center, who studies sweet taste and its evolution.

“In nature, sweetness tells you there are calories in there; that’s why animals respond so positively to sweet things. One of the most important things an animal has to do all the time is to make sure to have enough energy,” Beauchamp says. The presence of sweet taste, particularly when bitter tastes are absent, is associated with safe, calorie-dense foods containing sugars like glucose. In short, we were built to crave sugar.

If sugar cravings are at the root of our troublesome diets, it’s remarkable how few proven tools exist to reduce them.

One is a plant, called Gymnema sylvestre, that contains sweet-taste-blocking compounds. Gymnema has long been used in Ayurvedic medicine, with its origins in Southeast Asia. The Hindi word for the plant means “destroyer of sugar.” Research on the plant shows that the molecules responsible for its ability to shut down sweet-taste receptors are gymnemic acids, of which dozens exist in the plant.

Consumers can buy products featuring an extract of Gymnema, “but it is one of the most vile substances you will ever taste,” says Cara Cesario, an organic chemist and chief scientific officer at Sweet Defeat, which has commercialized a lozenge based on Gymnema to help people cut down on sugar and sweet cravings.

When Cesario joined Sweet Defeat 5 years ago, she was tasked with obtaining palatable Gymnema compounds that retain the sweet-blocking effect. Cesario quickly determined that isolating a single gymnemic acid would be expensive and impossible to scale up. But by deploying plant extraction techniques used in the food industry, she was able to obtain a high-purity extract of several gymnemic acids. Her process removed tannins and polyphenols that contribute a strong, lingering bitterness. The purified extract was still bitter, but manageable so.

The next task was to formulate the compounds into a lozenge so they are delivered to sweet-taste receptors on the tongue, where they would act as an antagonist. This C&EN reporter, after trying the lozenge, can confirm that it blocks the ability to taste the sweetness of Halloween candy for roughly an hour.

Clinical trials of the lozenge versus a placebo showed that, in addition to blocking sweet taste, the lozenge reduced overall sugar intake. In other words, it decreased cravings. Whether or not study participants were given candy before they tried the lozenge, their desire for candy after they had the lozenge was significantly reduced for the brief period of the study.

A follow-up study using functional magnetic resonance imaging showed that the lozenge reduced the reward response in the brain that is normally triggered by eating high-sugar food—in this case, a chocolate milkshake. It also reduced reward-region activity that is normally triggered when a person merely views a photo of a milkshake, the so-called anticipation response (Physiol. Behav. 2018, DOI: 10.1016/j.physbeh.2018.07.012).

More research is needed to see whether people who wish to reduce their sugar intake would use the lozenge over a long enough period of time to meaningfully change their habits. As a chemist, Cesario would also like to know whether the Gymnema molecules can be synthesized and improved.

For now, Cesario says Sweet Defeat can provide a temporary break from the cycle of sugar cravings. “Let’s do something to buy people some time so they don’t have to go right into the cabinet for a sweet snack after work,” she says. “That can be a small victory for someone and would make me very happy.”
& Lyle. Also called d-psicose, allulose intrigued researchers because it is a naturally occurring monosaccharide with only 0.4 calories per gram, one-tenth the calories of sugar.

As with stevia, it took a lot of innovation to figure out how to scale up a substance that occurs in only small quantities in plants. Starting about 15 years ago, rare-sugar experts at Japan’s Matsutani Chemical Industry collaborated with researchers at Kagawa University on an enzymatic transformation of fructose into allulose.

Matsutani’s process is based on an enzyme called d-allulose 3-epimerase, made with a gene borrowed from a strain of the soil bacteria Arthrobacter globiformis. Ingredion has partnered with Matsutani to produce allulose at a plant in Mexico. Tate & Lyle and South Korea’s CJ CheilJedang are also making the low-calorie sugar from cornstarch-derived fructose using their own patented enzyme processes.

Allulose is considered generally recognized as safe by the FDA, though it is not yet approved in the European Union. And it’s got a host of attributes that Storms eagerly lists. “In the clinical work we’ve done we show that it is absorbed but not metabolized, so it has negligible calories, it has no effect on glycemic response, and does not promote cavities,” she says.

Yet in 2015, Tate & Lyle faced the prospect that allulose would be listed as an added sugar on the new Nutrition Facts label, making these attributes hard to see. “The label would be very confusing to consumers, including people with diabetes,” Storms says.

Tate & Lyle gathered up all the evidence for treating allulose as a different kind of sugar, submitted it to the FDA, and waited. Four years later, the FDA published guidance saying allulose won’t be considered a sugar or an added sugar for purposes of the Nutrition Facts label. Rather, it will be included in the label’s Total Carbohydrates line, where it will have only a tiny caloric impact on the percent daily value.

“April 17 was a big day for us,” Storms says. “Many people said for us to call them as soon as our petition was granted, as many of their product development efforts were being held back because of the sugar figure. We had a long call list to go through that day.”

Tate & Lyle has been working with Quest Nutrition on Quest’s line of ketogenic-diet-focused protein bars. The company’s vanilla-caramel Hero bar gets its sweet taste from allulose, erythritol, and sucralose. Sucralose helps boost the over-all sweetness because allulose and erythritol are each only 70% as sweet as sugar.

Allulose and erythritol may duke it out for a while, or they may continue to coexist in the same products. Although allulose is new, it’s already cost competitive with erythritol, according to Storms. And it has a big advantage in that it tastes just like sugar and does not add a cooling effect, as erythritol does. It can be used in difficult high-sugar applications like chocolate and caramel because of its crystalline structure and ability to brown like sugar in the Maillard reaction.

The breakthroughs in allulose manufacturing and the FDA labeling guidance have come at a particularly advantageous time, Storms says, and not just for Tate & Lyle. “Consumers are just now looking at both calories and added sugar with an equal level of interest. There is a sizable proportion of people in the US and around the world who have diabetes or prediabetes,” Storms points out.

Public health experts want food companies to reformulate their offerings to benefit both the health-conscious and the carefree shopper. It’s tricky to take out sugar, but thanks to investments in sweetener innovation, it should soon get a little easier.