Taking the Bitterness out of the Health and Wellness Boom

A look inside the high throughput screening, validation and application process for bitter blockers

According to a recent report by The Freedonia Group, flavors and flavor enhancers accounted for $2.4 billion of the $7.2 billion US food and beverage additive market.[a] According to the report, growth through 2019 "will be driven by increasing consumer interest in nutritionally enriched products and all-natural foods, which promotes demand for high-value premium and natural additives." In addition to innovations in enhancers for salt reduction/replacement, the report adds, "[T]he constant emergence of new food and beverage products continues to create new demand for flavors and enhancers. The inclusion of functional additives such as probiotics in a widening array of foods and beverages"—including breakfast cereal, tabletop sweeteners, milk, chocolate, bread, nutrition bars, yogurt, juice and other beverages—"will benefit demand in this segment, as these nutraceuticals are often associated with a bitter taste that must be masked by flavor additives."

As the demand for effective bitter blockers has expanded in recent years, flavor companies have refined their research and discovery programs to more efficiently serve the market. Ioana Ungureanu, a research scientist at Givaudan Flavors, notes that classic bitter blockers used by flavorists "were discovered by trial and error." Today's process, she explains, is "much, much more efficient," adopting a high throughput screening process first innovated by the pharmaceutical industry.

The program Ungureanu is involved in screens compounds against a subgroup of the 27 receptors that in humans are associated with bitterness. "The activation of these bitter receptors is clearly linked to bitter taste," she says. "With this targeted subgroup of bitter receptors we are able to taste a huge number of bitter substances. It's very diverse. All kinds of molecules taste bitter."

In pursuing the discovery of bitter blockers via high throughput screening, the best candidates resulting from those screenings are validated via taste tests. Throughout the evolution of this process, Ungureanu says, "there are certain things we learned—especially the importance of eliminating things [bitter-blocking compounds] that have no chance from the very beginning. For us the initial work is very important because we want to remove what we call toxiphoric moieties—the toxic compounds."

Applicability, too, is a factor. "We have great bitter-blocking compounds, but they're not going anywhere because they're not soluble. We have to think of things with the end application in mind. You really want know in which applications these work—and do they block something other than bitterness? It took us time to learn this."

The likelihood of success for any one bitter-blocking compound is of course small. "You want to keep feeding the pipeline, because for different reasons most of those [materials] fail at one step or the other," says Ungureanu.

She notes that when the company launched its bitter blocking program, one of the first things researchers examined was artificial sweeteners. According to the Freedonia Group report, aspartame will continue to be the most popular "alternative sweetener" in the United States—particularly due to its use in soft drinks. "However," the report adds, "more rapid gains will be achieved by sucralose, acesulfame potassium (ace-K) and certain polyols. Additionally, trends favoring natural products will bode well for stevia sweeteners."

Givaudan's researchers long ago realized that the off notes associated with artificial sweeteners posed the greatest drawback to their popularity. Complicating matters further is the belief—shared by Ungureanu and other researchers—that genetic variations among humans may lead to bitterness registering differently among different consumers. "We know that one-third of the population doesn't like artificial sweeteners," says Ungureanu. "There are many soft drinks users that would like to switch to artificially sweetened [diet] soft drinks, but they cannot stand the taste."

Among their first key findings via Givaudan's bitter blocker screening activities was the matching of saccharin bitterness with the bitter receptor hTAS2R44. "Last year we [Givaudan] launched a bitter blocker which was originally designed to block saccharin [off notes]. Through research"—conducted by Givaudan, the German Institute of Human Nutrition Potsdam-Rehbruecke, the University of New Mexico School of Medicine and the Romanian Academy's Institute of Chemistry—"we discovered that the degree of generality was much greater than anticipated.[1]

[a] *www.freedoniagroup.com*

It also works with sucralose, vitamins and soy products. This pushed us to try to commercialize it faster." The other advantage? It is effective at a relatively low concentration.

As Ungureanu noted earlier, nothing moves very far in the screening process without being tested with flavorists at the bench: "When we find something [of interest] we immediately bring it to the flavorists. They have early exposure to these things. This is very interesting for us because it gives us an immediate reality check. The ingredients will have to be compatible with the flavor. You don't add them in separately." At the same time, ingredients such as saccharin suffer from not just bitterness, but also metallic notes and texture/body issues. And so candidate bitter blockers may need to work in collaboration with several additives, in addition to flavor materials. Flavorist input is crucial—particularly as the range of applications expands.

"The original intention of the bitter blocking program was [application] in soft drinks," says Ungureanu. "Then, as we progressed, we saw that they were very useful also for dairy products, artificially sweetened yogurts, energy drinks, low calorie products, etc. Our applications group tries to go as wide as possible. There are certain applications in which [blockers] work better, so that's why we keep searching for other ingredients."

When asked about what researchers hope to achieve in the coming years, Ungureanu discusses the advantage of compounds that block multiple bitter causing agents. "What we are looking for are ingredients that block three, four or five bitter compounds," she says, adding that something that can be applied more universally is unlikely. Meanwhile, Ungureanu and her colleagues are working to increase the number of natural bitter blockers in the company's pipeline. "The Holy Grail would be natural [blockers] compatible with all applications and with a long shelf life," she says.

Meanwhile, collaboration with flavorists drives new innovations. "We try to address the challenges that are coming in close relation with the flavorists, which enables us to see how fast the market is changing and to address every issue. [Rebaudioside A] was one of these examples. Once it was approved for use as a sweetener, the flavorists were immediately involved in the discovery process for bitterness blockers." As a result, Givaudan identified and applied for patents related to its discovery of the bitter taste receptor triggered by rebaudioside A.

References

1. JP Slack, A Brockhoff, C Batram, S Menzel, C Sonnabend, S Born, M Mercedes Galindo, S Kohl, S Thalmann, L Ostopovici-Halip, CT Simons, I Ungureanu, K Duineveld, CG Bologa, M Behrens, S Furrer, TI Oprea and W Meyerhof, Modulation of Bitter Taste Perception by a Small Molecule hTAS2R Antagonist. *Current Biology*, **20**, 1104–1109 (2010).