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Engineering Sweetness After Sucrose

Molecular Design, Enzymatic Bioconversion, Rare Sugars, Sweet Proteins and the European Regulatory Frontier

INTABIOTECH KNOWLEDGE CENTER

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An original interdisciplinary review of molecular taste science, industrial food engineering, human evidence and EU regulatory conditions.

Abstract

Sugar reduction is commonly approached as a substitution problem: the technologist removes sucrose, selects a high-intensity sweetener and restores sweetness until the analytical specification has been met. This interpretation is inadequate because sucrose performs at least four simultaneous functions in foods: sensory signalling, bulk and osmotic structuring, physicochemical control, and participation in chemical reactions during processing. Contemporary ingredient biotechnology offers a more complex repertoire, comprising highly purified steviol glycosides manufactured through enzymatic conversion, low-abundance monosaccharides such as D-tagatose and D-allulose, fermentation-derived polyols, and intensely sweet proteins. These ingredient families cannot be treated as interchangeable. Their metabolic fate, sweetness kinetics, solvent behaviour, thermal robustness, microbiological implications and legal identities are distinct. In 2026, a systematic review of 20 controlled human trials involving 1,033 participants reported attenuation of acute postprandial glycaemic responses after allulose or tagatose exposure but did not establish consistent benefits for longer-term lipid or body-composition outcomes. At the same time, the European regulatory position diverges sharply between authorised D-tagatose and D-allulose, for which EFSA was unable to establish safety on the dossier available in 2025. A Commission amendment adopted in October 2026 further illustrates how production-route specificity matters for enzymatically produced rebaudioside M. This article integrates receptor-level taste science, reaction engineering, formulation thermodynamics, analytical control, clinical evidence and European food law. It proposes a decision architecture for developing reduced-sugar foods whose performance is assessed as a coupled technological, physiological, sensory and regulatory system rather than by sweetness equivalence alone.

Keywords: *sucrose reduction; sweetener engineering; rebaudioside M; steviol glycosides; enzymatic bioconversion; D-tagatose; D-allulose; sweet proteins; thaumatin; sensory kinetics; food law; European Union; process design*.

1. Introduction: the inadequacy of sweetness equivalence

The ability to obtain a sweetness response comparable to a 10% sucrose solution does not mean that an ingredient will replace the function of sucrose in a beverage, a baked matrix or a protein-enriched snack. Sucrose contributes a concentration-dependent taste signal, an almost instantaneous onset relative to many high-potency sweeteners, characteristic temporal decay, perceived body and specific interactions with acid and aroma. It also modifies water activity, freezing-point depression, boiling behaviour, osmotic pressure, glass transition, crystallisation kinetics and the texture of concentrated aqueous systems. During heating, it can participate in caramelisation and, after inversion or hydrolysis, influence Maillard-associated chemistry through the resulting reducing sugars. Replacing sucrose therefore modifies a network of interacting variables, not a single ingredient line on the formulation sheet.

The commercial temptation to describe every alternative as natural, low-calorie, microbiome-friendly or metabolically advantageous is especially problematic. A compound may taste sweet without meeting the legal definition of a food-additive sweetener; another may be authorised as an additive but only for specified food categories and maximum levels. A highly purified molecule can be chemically indistinguishable from a botanical constituent yet require a separately assessed manufacturing specification. An acute reduction in postprandial glucose cannot, without further evidence, support a claim that long-term glycaemic control, cardiovascular risk or body mass will

improve. For the European food industry, the regulatory route must be considered at the outset of product design rather than after the sensory formula has been fixed.

This review accordingly advances a central proposition: successful sugar reduction requires the deliberate distribution of sucrose's functions among several compatible technological mechanisms, followed by analytical and clinical substantiation appropriate to the intended claims. The purpose is not to promote one sweetener class as universally superior. It is to create a scientifically credible method for choosing among them while acknowledging uncertainty, process-dependent safety, and the legal asymmetry between jurisdictions.

2. Scope, evidence classification and limitations

The article is a critical narrative review incorporating current systematic evidence and primary European regulatory documents, not a prospectively registered systematic review or an original clinical trial. Its evidence cut-off is 18 November 2026. Priority is assigned to EFSA scientific opinions, European Union legislation, human intervention research, systematic reviews and relevant peer-reviewed work on sweetener structure and sensory properties. Secondary commentaries are used only where they clarify technological questions; they do not substitute for primary authorisation records. Inferences concerning future applications are identified as engineering proposals rather than demonstrated clinical effects.

Four distinct evidentiary domains are maintained throughout the analysis. **Molecular plausibility** concerns receptor binding, enzymatic specificity and biochemical fate. **Technical performance** concerns manufacturability, ingredient purity, shelf life and sensory reproduction. **Human clinical evidence** concerns outcomes measured in appropriately controlled interventions. **Regulatory admissibility** concerns whether the exact material, produced by the exact process and used for the specific purpose, can lawfully be incorporated in the intended European food category. Positive evidence in one domain does not automatically satisfy the others. This separation is particularly important when using results obtained outside Europe or for a different source organism, bioconversion route, molecular profile or formulation matrix.

3. Sweet taste transduction and why kinetic profiles matter

Human sweet perception is principally mediated by the heterodimeric T1R2/T1R3 receptor, a class-C G-protein-coupled receptor expressed in taste-receptor cells. Binding by structurally different agonists activates downstream signalling involving G-protein pathways and cellular depolarisation, but the perceived result is not determined solely by receptor affinity. Concentration, oral residence time, pH, temperature, saliva, aroma, texture, cross-modal interactions and individual sensory sensitivity modify the psychophysical response. Receptor activity is therefore a useful mechanistic descriptor, but it is not a sufficient substitute for product-level descriptive sensory testing.

Sucrose delivers a distinctive temporal pattern: rapid onset, rounded sweetness and a relatively clean decline. Depending on the composition and concentration, certain steviol glycosides may produce delayed onset, persistent sweetness, liquorice-like notes or bitterness. Other glycosides, including rebaudioside M and rebaudioside D, have attracted considerable technological attention because purified profiles can improve sensory quality relative to older steviol-glycoside mixtures. They remain context-dependent; a favourable profile in water may not persist in an acidic beverage containing citric acid, sodium ions, caffeine, botanical extracts or high levels of protein.

A practical sensory model should describe at least the following parameters separately: detection threshold, perceived sweetness intensity at a defined sucrose-equivalent concentration, onset time, time to maximum sweetness, post-swallow persistence, bitterness, astringency, metallic or liquorice notes, and interaction with the target aroma. In industrial development the data should be derived from trained panels using validated intensity scales, followed by consumer confirmation in the actual packaged food. One-number descriptions such as '300 times sweeter than sugar' are inadequate as formulation specifications: relative sweetness changes with concentration, matrix and testing methodology.

Cross-modal compensation is of considerable practical importance. Acidulants can sharpen fruit flavour while changing perceived sweetness; sodium and selected salts can modulate bitterness; aroma congruency may increase sweetness expectations even when the concentration of sweetener is unchanged. These effects can create sensory opportunities, but they must be validated rather than presumed. A strategy based on aroma enhancement should also be assessed for possible flavour-profile drift over storage and under different serving temperatures.

4. The technology of enzymatically produced steviol glycosides

Steviol glycosides share the steviol aglycone yet differ in the number, identity and attachment of carbohydrate residues. The glycosylation pattern affects sweetness potency, temporal profile, solubility, sensory aftertaste and, potentially, the technical feasibility of purification. Leaves of *Stevia rebaudiana* contain a heterogeneous collection of glycosides, including compounds such as stevioside and rebaudioside A, whereas some of the most sought-after glycosides are naturally present in limited amounts. This creates a rationale for controlled bioconversion rather than relying on extraction alone.

Enzymatic manufacture can use glycosyltransferase activities, nucleotide-sugar recycling and tailored reaction conditions to convert purified steviol glycosides into a specified product, notably rebaudioside M. From a process-engineering perspective, a successful route must satisfy several constraints simultaneously: enzyme selectivity, substrate conversion, cofactor recycling, substrate and product solubility, formation of unwanted glycoside congeners, enzyme removal, downstream purification, and reproducible analytical composition across batches. Reaction yield alone is an insufficient optimisation target if the product cannot reliably meet additive specifications.

A particularly relevant example is Commission Regulation (EU) 2026/2309 of 16 October 2026, which amends specifications in Regulation (EU) No 231/2012 for rebaudioside M produced by enzymatic conversion of highly purified rebaudioside A using enzymes obtained from the genetically modified yeast *Komagataella phaffii* CGMCC 7539 within the defined E 960c(ii) route. This is a specification-level development, not a blanket authorisation for any fermentation-derived sweet compound or for any genetically engineered production organism. The precise identity of the substrate, enzyme-producing strain, manufacturing process and purified product remains relevant to compliance (European Commission, 2026; EFSA FAF Panel, 2025).

The industrial significance lies in the distinction between the **production organism** and the **marketed additive**. A genetically modified microorganism may be used to produce an enzyme, while the final food additive is a purified steviol glycoside subject to compositional and purity requirements. However, neither biochemical equivalence nor a statement that 'no live microorganisms remain' automatically resolves the entire regulatory assessment. Conditions governing detectable cells and DNA, process-related impurities and the accepted specification depend on the authorised route and

corresponding dossier. Food business operators must maintain traceability to the authorised additive specification, not merely to a commercial name such as Reb M.

Bioconversion should therefore be assessed through an integrated release specification comprising molecular identity and glycoside profile by validated HPLC or LC–MS methods; residual carbohydrate and process impurities; relevant metals and microbiological limits; moisture and stability; and process-specific criteria for production-organism residues where required. Acceptance of one rebaudioside M route cannot be extended, by assumption, to a different enzyme system or production strain. This is not a regulatory impediment to innovation but a reminder that novel manufacturing efficiency and food safety documentation must advance together.

5. Rare sugars: chemical similarity does not imply physiological equivalence

Rare sugars are monosaccharides occurring naturally at low concentrations or accessible through selective chemical or biological conversion. D-allulose (also called D-psicose) is a C-3 epimer of D-fructose; D-tagatose is a ketohexose with a different stereochemical relationship to more common dietary sugars. These subtle differences can alter intestinal absorption, metabolism, gastrointestinal tolerance and the interaction with metabolic responses to a carbohydrate load. Unlike high-intensity sweeteners, rare sugars can contribute meaningful bulk, solids and colligative properties, although their technological behaviour is not necessarily identical to sucrose.

Allulose has gained attention because of its sugar-like appearance and organoleptic functionality, including its usefulness in formulations requiring bulk. Tagatose is similarly valuable as a reduced-energy carbohydrate with sweet taste and relevant processing chemistry. Their production pathways may involve epimerases or isomerases and must address the thermodynamics of reaction equilibrium, catalyst stability, substrate sourcing, selective conversion, separation of structurally similar monosaccharides and removal of undesired by-products. A process that produces acceptable laboratory yields may still have poor industrial economics if chromatographic recovery, concentration, crystallisation or solvent management dominates total cost.

The simplest engineering comparison is not potency against sucrose, but **functional yield per kilogram of approved final ingredient**. This encompasses conversion selectivity, purification losses, energy demand for downstream processing, food-safety characterisation and performance in the target matrix. For a rare sugar, reducing manufacturing cost while generating a different impurity profile may change the regulatory identity of the commercial material. This is especially relevant to food ingredients assessed under a defined novel-food application and specification.

The distinction between molecular identity and commercial admissibility becomes decisive in Europe. D-tagatose is listed as an authorised novel food subject to applicable specifications and labelling provisions in the Union list under Implementing Regulation (EU) 2017/2470, as amended. D-allulose does not enjoy an equivalent general European market authorisation merely because it is sold in other jurisdictions. EFSA's 2025 scientific opinion on an application for D-allulose concluded that its safety could not be established from the available information, explicitly pointing to unaddressed data gaps concerning identity, manufacture, intended uses, genotoxicity and human information (EFSA NDA Panel, 2025). This outcome should not be misrepresented as a demonstration that D-allulose is inherently unsafe; it is a finding of insufficient information to establish safety for the assessed dossier. Conversely, a favourable foreign regulatory status is not an EU authorisation.

D-tagatose also illustrates the complexities of nutritional-energy calculations. An EFSA assessment in 2016 derived approximately 3 kcal/g (12.5 kJ/g) as an appropriate rounded metabolisable-energy factor on the evidence then reviewed. Whether and how that scientific opinion is reflected in an applicable product's mandatory EU energy declaration must be checked against the legislation and competent-authority interpretation; scientific opinions must not be treated as self-executing amendments to labelling rules. Furthermore, a monosaccharide cannot automatically be described as a non-sugar for EU nutrition-claims purposes simply because its glycaemic response differs from that of sucrose.

6. What controlled human intervention evidence shows nowadays

A systematic review and meta-analysis published in *The American Journal of Clinical Nutrition* in 2026 assessed 20 controlled trials involving 1,033 participants: 12 studies examining allulose and eight examining tagatose. The synthesis reported attenuation of acute postprandial glycaemic responses, with evidence also suggesting changes in acute insulin responses. However, it did not establish consistent meaningful improvements in long-term blood lipids or body composition, while some outcomes were supported by lower-certainty evidence. These findings support further investigation of acute metabolic functionality, not a general therapeutic proposition applicable to every sugar-reduced product (Glycemic and cardiometabolic effects, 2026).

Several methodological considerations deserve emphasis. The control comparator may differ across trials: water, glucose load, sucrose, an alternative sweetener or a complete meal. When a rare sugar replaces part of the digestible carbohydrate, a reduction in glycaemic exposure may arise partly from lower available-carbohydrate load, not necessarily from an additional pharmacological-like action of the rare sugar. An appropriate trial should therefore separate **substitution effects** from **ingredient-specific metabolic effects**. This may require isocaloric or carbohydrate-matched arms as well as realistic product comparators.

Similarly, an improvement in postprandial incremental area under the glucose curve does not necessarily imply reduced HbA1c, weight loss or lower cardiovascular event rates. Endpoint hierarchy matters. Acute glycaemia is a short-term biomarker; HbA1c assesses a different timeframe; body composition depends on total dietary intake, energy balance and adherence; cardiovascular outcomes demand larger and longer investigations. Precision nutrition claims cannot be generated by extrapolating one endpoint to an unrelated clinical outcome.

The trials also differ in participant phenotype, baseline glucose metabolism, concomitant medications, product form and amount consumed. Gastrointestinal tolerance requires explicit attention: some poorly absorbed carbohydrate fractions can exert osmotic effects, and microbial fermentation can affect symptoms, especially at larger doses. Dose-response characterisation should therefore include gastrointestinal symptom scores and stool-related outcomes alongside glycaemic measurements. A formulation that performs well at a laboratory test serving is not automatically suitable for repeated daily consumption across age groups.

For manufacturers, the practical conclusion is to regard rare sugars as potential **sugar-reformulation technologies with testable metabolic properties**, not established interventions for chronic disease. Product-specific human studies may still be justified where claims or differentiated physiological performance are material to commercial positioning. The availability of a published meta-analysis does not eliminate the need to validate the actual product, population, dose and intended communication.

7. Sweet proteins: the return of structure to taste engineering

Naturally occurring sweet proteins demonstrate that an intense sweetness signal need not arise from a small carbohydrate-like molecule. Thaumatin, brazzein, monellin, mabinlin and related proteins differ in molecular size, amino-acid structure, stability and receptor interactions. Their attractiveness rests on exceptionally high sweetness intensity at low usage levels; nevertheless, they do not provide sucrose-like bulk and may display temporal profiles that need blending or aroma management. In complex matrices their behaviour also depends on proteolysis, unfolding, aggregation, interfacial adsorption, pH and thermal history.

Thaumatin (E 957) is the established European reference for this ingredient family, with use governed by food-additive conditions and specifications. It would be incorrect to infer from thaumatin's authorisation that all other sweet proteins are authorised or interchangeable. A systematic review published in *Molecules* in 2026 emphasised the incomplete and uneven allergenicity evidence for several candidate proteins, underlining the need for a systematic assessment appropriate to each individual molecule and production source. In-silico sequence similarity is a useful screening tool but cannot, on its own, establish the absence of allergenic potential (Hidayati et al., 2026).

Recent protein-engineering research adds an important dimension. A study first published online in November 2026 reported rationally designed variants of brazzein and thaumatin with enhanced thermostability, illustrating the capacity of molecular design to improve formulation robustness. Such work is scientifically relevant to processing challenges, but the performance and safety assessment of engineered variants cannot be inherited without qualification from the naturally occurring parent protein. A modified amino-acid sequence may alter processing resilience, degradation products, immunological interactions and legal identity; each of these must be examined in a proportionate risk assessment (Sweet proteins designed with increased thermostability, 2026).

Industrial production can proceed through plant extraction or expression in selected microorganisms, depending on the protein and market. The terms 'fermentation-derived', 'precision-fermented' and 'natural' carry different technical and sometimes legal implications. The host organism, vector and production conditions affect protein folding, post-translational modification, impurity profile and purification strategy. Scale-up economics should consider volumetric productivity, recovery yield, required purity, downstream equipment and batch-to-batch reproducibility, not just target protein titre. For high-intensity compounds, sensory consistency at parts-per-million levels can justify more demanding analytics than those used for conventional bulk carbohydrates.

8. Ingredient selection as a constrained optimisation problem

A technically sound sweetener selection process begins by identifying what the original sucrose system accomplishes in the food and what the revised product must preserve. Consider an acidic functional beverage. Removing sugar may reduce sweetness, perceived body, aroma continuity and overall liking while simultaneously changing osmotic pressure and acid balance. A high-intensity sweetener may solve the receptor-level problem but fail to recover mouthfeel. A bulk ingredient may restore solids while increasing viscosity, fermentability or total energy. The preferred formulation is not the one with the lowest theoretical sweetener cost, but the one meeting all functional and compliance constraints at a commercially acceptable total cost.

A multiobjective design can be expressed conceptually as minimising a weighted loss function: sensory divergence + technological deviation + regulatory risk + stability loss + unit cost, subject to

safety, compositional and market constraints. The weights must reflect the product strategy and cannot be universal. Sensory divergence can be estimated with time–intensity analyses and multidimensional trained-panel scores. Technological deviation may include pH, water activity, crystallisation, flow behaviour and microbiological shelf life. Regulatory risk should be treated as a **hard feasibility constraint** when a particular additive use or ingredient lacks authorisation; it cannot legitimately be offset by superior taste or lower cost.

The design process should compare single ingredients with blends while explicitly testing concentration interactions. Sweetener synergy is not a universal law. Apparent enhancement can depend on dose, matrix composition and evaluation method, and high-potency mixtures sometimes preserve undesirable persistence despite improving onset. Small-scale response-surface experiments can help screen combinations, but confirmed winners require replicated sensory work and shelf-life tests under intended storage conditions.

Table 1. Functional comparison of major sweetness-engineering classes

Ingredient family	Main technological contribution	Key constraints	EU compliance implication
Sucrose	Sweetness, bulk, osmotic action, browning chemistry	Energy and available sugar load	Conventional food ingredient; claims depend on final composition
Enzymatically produced steviol glycosides	Intense sweetness at low dosage	Temporal profile, solubility, process-specific impurity controls	E 960c conditions and precise specification must match material
D-tagatose	Sweetness with significant bulk and processing functionality	Gastrointestinal tolerance, chemical reactivity, energy accounting	Novel-food authorisation and applicable labelling requirements
D-allulose	Sucrose-like bulk and sweetness potential	Process validation; dossier gaps in EU safety assessment	Not presumed authorised for EU placement on market
Thaumatin	Very high sweetness intensity; potential flavour-modifying utility	Minimal bulking; matrix-specific stability and kinetics	E 957 authorised subject to applicable category conditions
Other sweet proteins	High-potency future ingredient candidates	Stability, allergenicity, process purity, cost	No generic authorisation inherited from thaumatin
Erythritol	Bulk and sweetness with cooling effect	Gastrointestinal threshold; exposure, crystallisation	E 968; dose and intended-use controls apply
Sucralose	Potent and relatively clean sweetness in many matrices	Heat-process conditions and permitted uses	E 955; 2026 EFSA assessment distinguishes current uses from proposed baking extension

9. Process and product chemistry: four application environments

9.1. Acidic beverages and mixed fruit drinks

Acidic beverages require an integrated assessment of pH, titratable acidity, buffering, soluble solids, sweetener stability and packaging. High-intensity glycosides can reduce added sugar but often change mouthfeel; the response should be measured in a real beverage containing the intended fruit acids, aromas and protein or mineral fractions. Heat treatment may modify acidity, colour and sensory quality even when the sweetener itself remains analytically detectable. Product trials should therefore measure glycoside profile before and after thermal treatment, storage under light and ambient conditions, and both immediate and delayed sensory perception.

For beverages containing soluble protein, sweetener design interacts with haze, protein aggregation, electrostatic interactions and aftertaste. A formulation that becomes more acidic when sugar is removed may destabilise protein components if the buffering system changes. Reproducibility requires controlling raw-material variation, pH drift and dissolved-solids composition. The resulting product may satisfy a sugar-reduction target but still fail consumer acceptance due to new protein bitterness or diminished aroma roundness.

9.2. Bakery products and thermally intense processing

Baking illustrates why substitution by sweetness equivalence alone is inadequate. Sucrose affects aeration, starch gelatinisation, water distribution, moisture retention and colour development. A high-potency sweetener may allow a reduction in sugar content but cannot substitute for bulk, nor necessarily for caramelisation or reducing-sugar pathways. Formulation engineers should define the role of carbohydrates, fibres, polyols, protein and hydrocolloids separately and test combined effects on specific volume, texture profile, moisture and shelf life.

The 2026 EFSA re-evaluation of sucralose provides a useful case in regulatory scientific reasoning. EFSA found that authorised uses remained safe at estimated exposures, maintaining an acceptable daily intake of 15 mg/kg body weight per day, but could not confirm the safety of a proposed extension to fine bakery wares because uncertainties remain concerning potential chlorinated reaction products under prolonged high-temperature conditions. It would be equally mistaken to present this as proof that all sucralose-containing foods are unsafe or as proof that high-temperature baking applications are automatically acceptable. The relevant process conditions and authorisation boundaries must be respected (EFSA FAF Panel, 2026).

9.3. Confectionery, coatings and protein bars

Confectionery systems depend on solids, glass transition, crystallisation and moisture migration. Polyols and rare sugars can change water sorption, cooling effect, stickiness and thermal behaviour relative to sucrose. In protein bars, sugar reduction also interacts with the age-hardening mechanisms of concentrated proteins, plasticisers and carbohydrate binders. Accelerated storage tests should not be interpreted without validation against real-time storage, because some crystallisation and mobility processes do not scale linearly with temperature.

Cocoa coatings add a further complication: particle size, fat-continuous phase composition, rheology and flavour release determine whether the system will remain processable. The sensory impact of a high-intensity sweetener embedded in a fat matrix can differ from its behaviour in water. Pilot trials should therefore test the actual coating process, not rely exclusively on aqueous sweetness data.

9.4. Fermented dairy and plant-based analogues

In fermented products, readily metabolised sugars may also serve as fermentation substrates. Substitution can affect acidification curves, microbial growth, flavour formation, redox balance and post-acidification during storage. A non-fermentable intense sweetener will not provide the same functionality as lactose or sucrose during microbial processing. A rare sugar's metabolization by a particular starter or contaminant must be tested rather than assumed. The product should be assessed for starter performance, texture, syneresis, microbial counts and finished-product sweetness at distribution temperature.

10. Safety, dose and exposure: beyond the misleading ‘natural versus artificial’ binary

Risk assessment is substance-specific, dose-dependent and use-dependent. Botanical origin does not guarantee safety, whereas synthetic manufacture does not imply an unacceptable risk. The available evidence should be interpreted within exposure patterns, specification purity, vulnerable populations and possible interactions among multiple sweeteners in an individual's diet. The appropriate comparison is between characterised substances and realistic consumption scenarios, not marketing categories.

EFSA's 2023 re-evaluation of erythritol (E 968) established an acceptable daily intake of 0.5 g/kg body weight per day based on gastrointestinal laxative effects, specifically diarrhoea as the critical endpoint. This figure provides a quantitative reference for exposure assessment; it should not be confused with a threshold establishing that larger individual intakes will necessarily cause symptoms, nor should it be used to dismiss concerns raised by separate observational or mechanistic literature on cardiovascular outcomes. Different research designs answer different questions, and causal inference remains central. For a 70-kg reference adult, 0.5 g/kg corresponds arithmetically to 35 g per day, but vulnerable subgroups and cumulative exposure from multiple foods require additional consideration (EFSA FAF Panel, 2023).

The World Health Organization's 2023 recommendation against relying on non-sugar sweeteners for long-term weight control is a population-level, conditional guideline; it is not a toxicological judgment that reverses existing individual additive authorisations. The WHO's defined scope excludes some low-calorie sugars and sugar alcohols. At the level of food innovation, reduced sugar can remain a legitimate formulation and dietary objective even when there is insufficient evidence to promise long-term weight reduction from sweetener consumption as such (WHO, 2023).

For rare sugars, gastrointestinal tolerability must be tested at realistic serving sizes and repeat-use patterns. For sweet proteins, allergenicity assessment should integrate sequence analysis with relevant experimental evidence and exposure considerations. For bio-converted glycosides, process impurities, identity and potential residues are primary safety questions. Each class creates a different critical-control profile; a single generic ‘clean label’ dossier cannot replace material-specific assessment.

11. European legal architecture: the exact route matters

European authorisation is not a blanket recognition of sweet taste. It is a legal determination based on the identity and category of a substance, the intended technological function, specified food categories, use levels, purity requirements and applicable food information obligations. The baseline framework includes Regulation (EC) No 1333/2008 for food additives, Commission Regulation (EU) No 231/2012 for specifications, Regulation (EU) 2015/2283 and Implementing Regulation (EU) 2017/2470 for novel foods, Regulation (EU) No 1169/2011 for consumer information and Regulation (EC) No 1924/2006 for nutrition and health claims.

The same compound can raise different questions depending on how it is marketed and used. A food additive functioning as a sweetener must be authorised for the relevant food category and comply with restrictions. A novel carbohydrate used as a food ingredient may require a novel-food authorisation and specific labelling even when it is not an additive sweetener. A process produced with genetically modified microorganisms requires attention to authorised ingredient specifications

and other applicable provisions; claims of genetic-engineering-free status must be reviewed against the actual manufacturing history and legal definitions, not inferred from purification alone.

Label design creates frequent errors. Under Annex III of Regulation (EU) No 1169/2011, a food containing an authorised sweetener must bear the applicable statement 'with sweetener(s)' accompanying its name, or 'with sugar(s) and sweetener(s)' where both added sugars and sweeteners are present, as applicable. Further special statements can arise for polyols and particular sweeteners under their stated conditions. An ingredient permitted in the formula does not automatically permit its preferred marketing description.

Claims concerning sugar require equally careful calculations. Under Regulation (EC) No 1924/2006, 'sugars-free' has a maximum threshold of 0.5 g of sugars per 100 g or 100 mL. 'Energy-reduced' requires a reduction of at least 30% relative to appropriate comparable products, together with an indication of the characteristic responsible. 'With no added sugars' requires that no mono- or disaccharides or other foods used for their sweetening properties be added; naturally present sugars require the relevant accompanying indication. Adding a monosaccharide with a lower glycaemic response should not be assumed compatible with the 'no added sugars' claim. The separate 'reduced sugars' claim is also subject to its own conditions, including an energy comparison in the legislation as applicable.

The availability of some authorised health claims regarding sugar replacers and postprandial glycaemic response does not entitle a manufacturer to attach arbitrary claims to a product. The applicable authorised wording, sugar-replacement conditions and category-specific restrictions must be examined, particularly under Commission Regulation (EU) No 432/2012 and its amendments. Evidence that a novel ingredient changes a metabolic biomarker does not itself constitute regulatory authorisation to advertise that effect. Product developers should perform a claim-by-claim legal assessment before public communication.

Table 2. EU regulatory decision points for a 2026 sweetener project

Decision point	Evidence required	Decision consequence
Substance and commercial material identity	Identity, stereochemistry or glycoside profile; specifications; source and production method	Determines whether the correct authorised entry has been identified
Regulatory category	Food ingredient, authorised additive or novel food; intended technological function	Determines the premarket route and conditions of use
Manufacturing provenance	Enzyme source, strain where relevant, purification and impurity controls	Verifies correspondence to authorised specification, including E 960c variants
Food category and dose	Product classification, maximum permitted level or quantum satis where applicable	Establishes use legality for the actual application
Exposure and safety	Estimated per-serving and total dietary exposure; population; relevant ADI	Supports risk assessment at realistic consumption levels
Food information	Ingredient designation; mandatory sweetener statements; energy and sugar calculations	Controls truthful labelling under Regulation 1169/2011
Intended claims	Claim wording, authorised conditions, comparative basis and evidence	Determines legality under Regulation 1924/2006
Jurisdiction and launch date	EU/GB/other market differences and current consolidated legislation	Prevents reliance on foreign approvals or superseded rules

12. Analytical verification and a proposed industrial quality system

A modern sweetener programme needs an analytical strategy linked to critical quality attributes, not simply a certificate of analysis containing a single assay percentage. For steviol glycosides, the profile of principal glycosides and manufacturing impurities should be established using validated chromatography suitable for the range of congeners present. For rare sugars, assays need to distinguish epimers and structurally related carbohydrates and should examine unwanted substrates, degradation products, moisture and relevant chemical impurities. For sweet proteins, validated purity, identity, unfolding/aggregation status and microbiological controls can be necessary, together with source-specific process residues.

The methodological hierarchy should include identification, quantification, repeatability, intermediate precision, recovery, detection/quantification limits and matrix validation. Stress studies should cover processing and storage: heat, pH, oxygen, light and packaging interactions appropriate to the actual product. Importantly, **analytical retention is not equivalent to retained sensory performance**. A stable assay result may coexist with flavour changes arising from other ingredients; conversely, a minor chemical change can be disproportionately relevant where sweeteners operate at very low concentrations.

A practical release-to-launch system would integrate four gates. The first is a regulatory feasibility dossier before pilot spending. The second is a laboratory proof-of-concept with chemical and sensory endpoints. The third is a pilot or industrial validation under commercially representative processing conditions. The fourth is a product-specific exposure, labelling and claims sign-off, followed by real-time shelf-life monitoring. Suppliers should be qualified by manufacturing route and documentation reliability, not merely by commercial name and target price.

13. A proposed research programme for industrial sugar reduction

An analytically defensible research programme should be divided into linked work packages. The programme below is a proposed methodology, not a statement that any of the experiments have already been performed by INTABIOTECH or its partners.

Work package A - Molecular and material characterisation. Define the full chemical identity, production method, ingredient specifications and realistic regulatory status of each candidate. Establish soluble-solids contribution, relative sweetness under controlled conditions, pH-dependent behaviour, thermal degradation profiles and any measurable interaction with the target matrix. Include a validated reference formulation with sucrose and a second reference featuring a widely authorised sweetener system.

Work package B - Sensory kinetics and blend screening. Construct a designed experiment combining a small number of authorised sweeteners or ingredients at justified ranges. Measure sweetness time-intensity, aftertaste, bitterness, flavour balance and consumer preference. Use a blinded, randomised serving order and prevent high-potency sweetener carryover with adequate washout. Where concentrations differ substantially from historical recipes, measure not only overall liking but diagnostic attributes that explain rejection.

Work package C - Process engineering and stability. Subject selected formulations to realistic pasteurisation, aseptic processing, baking, conching or fermentation conditions as appropriate. Collect baseline and post-process samples and monitor chemical identity, aroma, texture, colour and microbiological stability. Combine accelerated screening with real-time confirmation, ensuring that

predictive shelf-life models have been calibrated for the formulation's water activity, pH and packaging.

Work package D - Nutritional characterisation. Determine analytically verified sugar composition, carbohydrate fractions and energy values using the legally applicable calculation method. Do not infer regulatory ‘sugar-free’ or ‘low energy’ status from ingredient marketing descriptions. Where a reduced postprandial response is an intended research objective, design a controlled human crossover trial with an appropriate comparator, pre-registered endpoints and a sufficient washout period. Consider baseline glucose phenotype and the difference between an ingredient-specific mechanism and a lower total available-carbohydrate exposure.

Work package E - Scale-up and regulatory translation. Review supplier qualification authorised additive or novel-food entries, exact specifications, conditions of use, import documentation, consumer labelling and advertising claims. Assess operating cost at the intended industrial volume, accounting for sweetener price, bulking system, processing losses, analysis, logistics and possible reformulation of aromas and stabilisers. The final decision should be based on technically successful **and lawfully marketable** product prototypes.

A useful early application is the acidic, protein-enriched beverage, where sugar replacement creates simultaneous flavour, pH and mouthfeel challenges. A second is the cocoa or protein coating, in which a different solid-phase architecture is needed to preserve flow properties and sensory quality. A third is a low-sugar fermented system, in which sweet taste must be designed independently from the carbohydrate source required by microorganisms. These examples span distinct physical environments and therefore provide a more stringent test of a platform approach than three variants of the same beverage.

14. Commercial opportunity and scientific discipline

The expanding range of enzyme-catalysed glycosides, rare carbohydrates and proteins can support a meaningful change in sweetener procurement and industrial partnerships. The value proposition increasingly resides in a specified process, controlled molecular composition and demonstrated behaviour in the customer's finished food rather than in generic claims of being natural or exceptionally sweet. For an ingredient company, technical differentiation can be created through validated grade selection, product-specific blend design, predictable performance after processing and credible regulatory assistance.

Nevertheless, technical novelty can create false business confidence when the route to EU authorisation is misunderstood. As of the November 2026 evidence cut-off, the possibility of using an ingredient in another market should not be confused with lawful EU placement on the market. Scientific publication may validate a concept without resolving the admissibility of the exact commercial material. Positive in-vitro or small-scale sensory results may not transfer to industrial manufacturing. The economic argument for a new sweetener is therefore strongest when its specification, legal pathway, sensory profile and supply reliability are known before claims or major commercial commitments are made.

Strategically, INTABIOTECH could use these insights to organise applied work within a sugar-reduction and sweetness-engineering portfolio. This would mean establishing the technological brief first and determining whether authorised steviol glycosides, permitted polyols, approved ingredients, bulk substitutes, aroma strategies and other compliant technologies are suitable to the matrix. Product-family names should never substitute for verified formulation specifications or regulatory

dossiers. Such a programme is a proposal for future validation, not a representation that any particular branded formulation is already demonstrated or approved for every application.

15. Conclusions

The most important development in sweetness technology is not the discovery of a single molecule capable of replicating sucrose. It is the ability to design systems in which molecular identity, production route, taste dynamics, bulk functionality, metabolic response and legal status are considered together. Enzymatically produced rebaudioside M exemplifies the increasing precision of bioconversion technology and manufacturing-specific EU specifications. Rare sugars exemplify the distinction between promising human metabolic signals and actual authorisation: D-tagatose and D-allulose cannot be placed in the same regulatory category merely because they are both ketohexoses with reduced postprandial glycaemic responses in clinical research. Sweet proteins demonstrate how protein engineering may extend the functional envelope of taste-active ingredients while creating additional questions about safety, stability and ingredient identity.

Three principles follow. First, sweetness equivalence is not formulation equivalence; process properties and finished-product sensory performance must be demonstrated. Second, an observed acute physiological effect should not be promoted as evidence of durable cardiometabolic benefit without longitudinal clinical support. Third, European marketability must be established for the exact ingredient, route and use, with legally defensible labelling and claims. When these principles are incorporated from the first design stage, sugar reduction can become a rigorous platform for food innovation rather than an exercise in ingredient substitution and promotional language.

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This review distinguishes published evidence from proposed applications. Regulatory statements reflect sources verified to 18 November 2026 and must be checked against the consolidated legislation before commercial implementation.

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