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# Dietary Nitrate and the Nitric Oxide Pathway

*Reengineering the Vascular Potential of Plant Foods*

***From the Entero-salivary Microbiome and Nitric Oxide Biochemistry to Clinical Evidence, Beverage Technology, Exposure Assessment and European Food Law***

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Critical interdisciplinary synthesis · Scientific evidence, industrial implications and European regulatory analysis

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## Abstract

Inorganic nitrate in vegetables occupies a scientifically unusual position. It is simultaneously a naturally occurring constituent of foods, an exposure considered in toxicological risk assessment, a substrate for an entero-salivary microbial pathway that contributes to nitric oxide production, and, when deliberately used for a technological purpose in specified food categories, a regulated additive. None of these identities can be substituted for another. This interdisciplinary review examines nitrate–nitrite–nitric oxide chemistry, the oral microbial contribution to nitrate reduction, heterogeneity in human vascular responses, the manufacture and stability of nitrate-containing vegetable beverages, analytical control, safety and European food law. Recent randomized investigations, including a 2026 acute dose-response trial using 200, 400 and 800 mg nitrate, show that improvements in arterial stiffness, endothelial function and aortic blood pressure need not follow the same dose–response relationship. Other 2026 studies examine the interaction of nitrate and betalains, cerebrovascular endpoints, and the consequences of oral antisepsis. Evidence remains outcome-, population- and preparation-specific: a change in plasma nitrite is not by itself a demonstrated reduction in cardiovascular disease; a favourable physiological trial does not create an authorized European health claim. Regulation (EU) 2023/915 establishes product-specific maximum nitrate levels for certain vegetables and foods for infants and young children, whereas Regulation (EU) 2023/2108 governs selected additive uses of nitrites and nitrates. An acceptable daily intake provides a reference for exposure assessment, not a universal product reformulation target or an automatic ban on an individual vegetable serving. The review develops a stage-gated industrial framework for raw-material selection, nitrate standardization, microbial control, processing, packaging, shelf-life verification, exposure assessment and lawful consumer communication. Its principal conclusion is that the industrial opportunity lies in evidence-defined vegetable ingredients, not in rebranding nitrate chemistry as a universal cardiovascular treatment.

**Keywords:** dietary nitrate; nitrite; nitric oxide; beetroot; oral microbiome; vascular function; endothelial function; blood pressure; betalains; vegetable juice; methaemoglobin; nitrosamines; processing; HACCP; EFSA; European food law; health claims.

## 1. A substance with several biological and legal identities

The same nitrate ion can enter a food business through different routes and generate quite different questions. It may be present in a freshly harvested beetroot because the plant has accumulated inorganic nitrogen during growth. It may remain in a juice after extraction and concentration. It may be deliberately introduced as a food additive for a narrowly defined technological purpose. It may also be measured as part of an environmental or dietary exposure assessment. Chemically these contexts involve $NO_3^-$; legally and practically they are not interchangeable.

This distinction has become especially important as vegetable-based products move from the produce aisle into small-volume concentrated shots, powders, sports-nutrition preparations and functional beverages. The scientific attraction is substantial. Nitrate can be reduced to nitrite and, under suitable conditions, contribute to nitric oxide (NO) production. NO participates in vascular signalling, including the relaxation of smooth muscle through soluble guanylyl cyclase and cyclic GMP. However, the existence of a plausible biochemical pathway does not demonstrate that every source, dose, delivery system or consumer population will receive the same physiological effect.

The scientific question for food technology is therefore not whether beetroot is intrinsically beneficial or hazardous. It is how a specified nitrate exposure, within a specified food matrix and manufacturing history, influences measurable biology while remaining safe, stable and lawful. An ingredient company should resist the temptation to infer clinical utility from a single assay of plant nitrate content. A product with excellent nitrate retention may still show unsuitable sensory performance, excessive variability, an inadequate safety dossier or a proposed health claim unsupported by EU authorization.

This review treats the nitrate paradox not as a rhetorical contradiction but as an example of the need to separate chemical identity, human response and regulatory classification. The analysis is a critical narrative synthesis, not a registered systematic review or an original intervention study. The scientific and legal cut-off is 19 November 2026.

## 2. The chemistry: nitrate is a reservoir, nitrite an intermediate and NO a signal

Nitric oxide is a reactive free-radical signalling molecule with a short lifetime in biological systems. The classical endogenous route is enzymatic: nitric oxide synthase (NOS) converts L-arginine and oxygen to nitric oxide and L-citrulline in a process dependent on cofactors and redox conditions. Endothelial NOS is central to vascular

physiology. The alternative nitrate–nitrite–NO route provides a complementary reservoir-and-recycling mechanism in which comparatively stable inorganic nitrate can, through microbial and host chemistry, ultimately yield NO.

Three chemical species should be distinguished at every stage:

**$NO_3^-$ (nitrate):** relatively stable under many aqueous food-processing conditions, but not invariant in microbiologically active matrices. **$NO_2^-$ (nitrite):** a more reactive intermediate whose formation and fate depend on microbial activity, oxygen, acidity and the surrounding chemistry. **NO (nitric oxide):** a signalling species generated through several enzymatic and non-enzymatic routes; its systemic effects are not measured directly by determining the nitrate concentration of a bottle.

The stoichiometric identities matter. One millimole of nitrate ion corresponds to approximately **62.0 mg $NO_3^-$**; one millimole of nitrite ion corresponds to approximately **46.0 mg $NO_2^-$**. The corresponding masses of sodium or potassium nitrate are greater because the counterion contributes to molecular weight. A product described as providing 400 mg “nitrate” should specify whether the number means nitrate ion, a nitrate salt or a mass of nitrate-containing extract. These expressions are not synonyms, and confusing them can undermine dose comparison across trials and products.

Conversion to NO is conditional. Acidic gastric chemistry can favour nitrite-derived nitrogen-oxide species. In tissues, several proteins and redox systems can contribute to nitrite reduction, especially when oxygen availability and pH differ from resting conditions. Conversely, nitrite can enter reactions leading to N-nitroso compounds in appropriate chemical environments. The balance depends on the food matrix, other reactants, antioxidants, processing, microbiological conditions and host physiology. Thus, the nitrate pathway cannot be described as automatically beneficial at all exposures or automatically equivalent to the nitrite chemistry of cured meat.

The most defensible mechanism diagram is a sequence with explicit conditionality: vegetable nitrate → gastrointestinal absorption → concentration of circulating nitrate into saliva → microbial reduction to nitrite in the oral cavity → swallowed nitrite and systemic nitrite pools → context-dependent formation of NO and other nitrogen species → a physiological response that must be tested in humans. Each transition is a candidate source of variability, not a fixed percentage conversion.

## 3. The oral microbiome is an active part of the delivery system

Dietary nitrate challenges the conventional division between food formulation and host microbiology. After intestinal absorption, a fraction of circulating nitrate is concentrated in saliva. Bacteria on the tongue and other oral surfaces possess nitrate-reductase capacity and can convert part of this nitrate to nitrite. The resulting salivary chemistry feeds into gastrointestinal and systemic nitrogen-oxide pathways. The product’s effective delivery mechanism is therefore partly located outside the bottle.

This is not evidence that nitrate should be marketed generically as a prebiotic. The term has a defined scientific meaning and does not automatically apply whenever a substrate changes microbial abundance or activity. It is more precise to describe nitrate reduction as a functional host–microbe interaction. Oral microbial communities differ across individuals, and genes, enzyme expression, tongue ecology, diet, oral hygiene and medication can influence the pathway. A count of a supposedly favourable genus is not a measurement of nitrate-reductase activity, just as an elevated plasma nitrate level is not proof of a clinically significant change in blood pressure.

A 2025 double-blind crossover intervention involving 15 older adults with treated hypertension compared four-week intake of nitrate-rich and nitrate-depleted beetroot juice. The work found an effect on oral microbial composition without an analogous clear change in intestinal microbial composition. The distinction is important: the relevant functional compartment is oral, and it would be scientifically unjustified to infer a generalized intestinal microbiome benefit from the exposure (Fejes et al., 2025).

A 2026 randomized pilot examined antiseptic mouthwash, nitrate-rich beetroot juice and their combination in 15 volunteers divided among small groups. The observations support the sensitivity of oral nitrate-reduction function to chlorhexidine exposure and the need to assess the host–microbial interaction rather than assuming that the supplement dose alone defines biological delivery. Because the groups were very small, the study is best read as mechanistic pilot evidence, not as a clinical directive to abandon prescribed oral antisepsis (Nitrate Sustains Oral Microbiome Function, 2026).

An additional 2026 preliminary randomized trial compared antimicrobial mouthwashes and monitored oral and blood-pressure-related measures. Together these studies underscore a methodological point: oral hygiene is a plausible modifier that should be documented in nitrate trials. However, decisions about dental infection prevention must not be displaced by speculative cardiovascular messaging. In clinical or industrial protocols, antiseptic exposure should be recorded or standardized where scientifically and ethically appropriate, not manipulated without healthcare oversight.

## 4. Why a nitrate dose cannot be read as a vascular outcome

The physiology of NO is multilevel. Increased circulating nitrite may indicate activation of part of the nitrate–nitrite pathway, but blood pressure is determined by vascular tone, cardiac output, fluid balance, autonomic control, medications, arterial stiffness and many other variables. Endothelial function measured by flow-mediated dilation is not the same outcome as ambulatory blood pressure; an acute change in central aortic pressure is not proof of a sustained clinical benefit; and plasma cyclic GMP may fail to change even when other measurements respond.

The 2026 trial of McLellan and colleagues is an instructive counterexample to a simplistic “more nitrate means more benefit” formulation. In a randomized, double-blind crossover study, participants consumed acute beetroot-derived nitrate doses of **200, 400 or 800 mg**, with cardiovascular measures made before and approximately 2.5 hours after dosing. Plasma nitrate and nitrite rose; arterial-stiffness measures improved after the tested nitrate doses without clear between-dose separation. Yet the reported endothelial-function signal was evident at **400 mg**, while the reduction in aortic systolic blood pressure was reported at **800 mg**. Brachial blood pressure and plasma cyclic GMP did not show corresponding changes. A single dose–response curve therefore cannot represent every vascular endpoint (McLellan et al., 2026).

There are at least three reasons for such divergence. First, the relation between exposure and effect may involve biological thresholds, saturation, time-dependent peaks and measurement variability. Second, the vascular compartment matters: conduit-artery endothelial behaviour, central pressure and peripheral cuff pressure are not identical physiological phenomena. Third, study size, baseline health, oral microbial functionality, recent diet and measurement timing can affect estimated response. Selecting the single most favourable endpoint after trial completion would create a misleading impression of consistency.

The broader literature contains meta-analyses of chronic nitrate interventions, but the ingredients included in each synthesis must be checked. A 2026 systematic review of **sodium-nitrate supplementation** expressly excluded beetroot-juice intervention studies. Importantly, that review pooled six randomized trials involving 181 participants and found no statistically significant chronic reduction in systolic or diastolic blood pressure or resting heart rate with isolated sodium-nitrate interventions at the doses and durations assessed. This negative finding must be reported alongside promising acute beetroot experiments: the datasets address related but non-identical exposures and outcomes. Results from juice studies cannot simply be represented as evidence for purified nitrate salts in a different food category, or vice versa. The source, counterion, co-constituents and dosing schedule are all part of exposure definition.

The proper experimental question is not whether nitrate “works”. It is which chemically characterized preparation, in which population, over which period, affects which prespecified outcome, relative to what comparator, with what uncertainty and safety profile.

## 5. The 2026 human evidence: promise, selective responses and significant limitations

Trials published in 2026 offer an increasingly differentiated picture. An August crossover pilot in 16 healthy participants compared two beetroot juices with very different measured profiles: one provided approximately **1,280 mg nitrate and 147 mg betalains**; the other **1,120 mg nitrate and 506 mg betalains**. The study followed six days of ingestion with additional acute measurements on day seven. Changes in circulating nitrate and nitrite and some vascular variables were observed, but they were not identical between preparations. The work is useful because it deliberately moves beyond equating any beetroot juice with a single nitrate dose. It cannot independently disentangle every ingredient effect, nor does a short healthy-volunteer study establish long-term cardiovascular-risk reduction (Effects of Nitrate- and Betalain-Rich Beetroot Juice, 2026).

A separate 2026 pilot randomized **22 older adults with metabolic syndrome** to four weeks of nitrate-rich beetroot juice providing **6.4 mmol nitrate per day** or nitrate-depleted placebo. The investigators examined dynamic cerebral

autoregulation using beat-to-beat pressure and near-infrared-derived cerebral oxygenation. The study demonstrates that cerebrovascular physiology can be investigated in a controlled design but also illustrates the limited interpretability of small pilots for cognitive or vascular clinical outcomes. Feasibility and biomarker exploration are different from proof of prevention of neurological disease (A Pilot Randomized Controlled Trial of Dietary Nitrate, 2026).

At the other end of the clinical spectrum, a November 2026 crossover pilot enrolled **eight older patients with coronary artery disease** in a short intervention with nitrate-rich or nitrate-depleted beetroot juice. The authors reported feasibility and promising endothelial observations, while explicitly calling for a properly powered trial. Eight participants cannot support a generalized therapeutic recommendation, and the findings must not be silently transferred to healthy populations, children or patients taking different cardiovascular medications (Soonhuae et al., 2026).

A 2026 crossover study in bodybuilders with a history of anabolic–androgenic steroid exposure identified biochemical and endothelial changes without corresponding improvement in all cardiovascular or strength outcomes. This is valuable negative or mixed evidence: an intervention can alter nitrate metabolism yet fail to reverse a distinct pathophysiological condition. Treating the biochemical mechanism as a guaranteed clinical endpoint would overstate what the trial measured.

**Table 1. Clinical evidence and the limits of permissible inference**

| Investigation | Controlled exposure or design | Observation supported | Unsupported extrapolation |
|---|---|---|---|
| McLellan et al., 2026 | Acute crossover; 200, 400, 800 mg nitrate | Endpoint-specific changes in stiffness, endothelial function and central pressure | Uniform dose response; proven reduction in clinical cardiovascular events |
| Beetroot nitrate/betalain pilot, 2026 | n = 16; two compositionally distinct juices; approximately six days | Different biomarker and selected vascular responses | Attribution of the entire effect to betalains or nitrate alone; long-term efficacy |
| Metabolic-syndrome cerebral pilot, 2026 | n = 22; 6.4 mmol nitrate/day; four weeks | Feasibility and exploratory cerebrovascular assessment | Prevention of dementia, stroke or cognitive decline |
| Coronary-artery-disease pilot, 2026 | n = 8; short crossover with nitrate-depleted placebo | Preliminary endothelial signal and tolerability in selected patients | Clinical treatment claim for coronary disease |
| Oral microbiome crossover, 2025 | n = 15; four-week nitrate-rich versus depleted juice | Oral microbial response under controlled conditions | General intestinal microbiome benefit or authorized health claim |

The table describes published interventions, not new clinical data generated by INTABIOTECH. Endpoints, statistical uncertainty and exact preparations must be consulted in the primary reports before quantitative synthesis.

## 6. The food matrix: beetroot is not purified nitrate

Beetroot contains multiple categories of constituents: nitrate, pigments including betalains, organic acids, minerals, sugars, soluble solids and other phytochemicals. Their relative amounts vary with cultivar, growing conditions, harvest timing, root size, irrigation, fertilization and post-harvest processing. A beetroot powder containing a particular nitrate concentration is not necessarily equivalent to a juice containing the same nitrate dose when osmolarity, viscosity, polyphenol composition, gastric emptying, sensory properties and co-exposure differ.

Betalains are attractive markers of beetroot identity, but they are not interchangeable with nitrate. Their colorimetric behaviour and sensitivity to oxygen, light, heat and pH differ from nitrate chemistry. A visually stable red product can lose nitrate under conditions in which microorganisms reduce it; conversely, a measured nitrate concentration can remain within specification while pigment degradation makes the beverage commercially unacceptable. A food developer who controls only one analyte has not established shelf-life quality.

The distinction becomes sharper in concentrated shots. A small serving may deliver a comparatively large quantity of nitrate with less of the volume and food structure associated with eating vegetables. This can improve dosing convenience and analytical reproducibility, but it alters exposure patterns. It should not be assumed that health-risk conclusions based on eating vegetables as part of a balanced diet automatically validate arbitrary concentrated products or dosing frequencies.

From a formulation perspective, nitrate should be measured independently from sugar and °Brix. Refractometry measures bulk soluble matter, not nitrate specifically. Red colour is not a valid surrogate. Likewise, measuring a

nitrate-containing powder by total nitrogen is insufficient to identify nitrate-ion dose. An ingredient technical specification should distinguish the botanical material, water content, nitrate ion, nitrite ion, sodium and potassium, microbial quality, relevant contaminants, pigments where material to product quality, and the analytical method used for each.

## 7. Processing and storage: microbiology can turn a stable assay into a moving target

The vegetable nitrate narrative has often concentrated on plant physiology while neglecting factory operations. Fresh juice extraction creates a nutrient-rich aqueous matrix. If hygiene, holding time and temperature are not controlled, microbial activity can change the balance between nitrate and nitrite. This is not merely a problem of diminished marketing potency. Nitrite accumulation changes chemical exposure and can become a food-safety question, especially in susceptible consumers and in products with unusual storage histories.

Bescos and colleagues measured nitrate and nitrite in commercial and self-prepared beetroot juices and investigated storage at **20 °C, 4 °C and −20 °C**, together with pH manipulation. In their experimental self-made juice, nitrate degradation was substantial at ambient temperature and markedly attenuated under refrigeration or freezing; an acidified preparation behaved differently. The findings should not be universalized as exact kinetic constants for all products, but they establish the need to measure both species throughout shelf life rather than treating the initial nitrate certificate as a permanent statement of composition (Bescos et al., 2023).

Pasteurization, aseptic filling, high-pressure processing or other preservation choices must be evaluated for the actual target beverage. Inactivation of unwanted microorganisms can help stabilize nitrate chemistry, but some processes may change sensory properties, pigment content, oxygen exposure or other quality attributes. A 2026 investigation of mild pasteurization of fermented beetroot juice reported product-specific observations over storage, yet a fermented beverage should not be assumed to share the same nitrate/nitrite trajectory as an unfermented concentrate. Process validation must preserve the distinction.

A defensible manufacturing flow should examine the following decision points: raw-beet reception, washing and trimming, maceration, juice extraction, pre-processing holding, thermal or nonthermal stabilization, filling, residual oxygen, package barrier, distribution temperature, opening by the consumer and in-use shelf life. Each step can affect microbial load or downstream chemical conversion. The critical control question is whether the target nitrate dose and an acceptable nitrite profile remain within specification under reasonably foreseeable conditions.

Concentrating a juice can increase the nitrate concentration per unit volume without necessarily improving its stability. Thermal evaporation or membrane concentration also changes sugar, mineral and pigment ratios; the operation should be evaluated as a mass balance. If a dry powder is manufactured, drying temperature, oxygen exposure, hygroscopicity, reconstitution behaviour and storage humidity enter the specification. None of these processes establishes a physiological health benefit by itself.

## 8. Analytical design: two ions, several matrices and a sampling problem

Ion chromatography is a powerful approach for nitrate and nitrite determination in appropriately prepared aqueous matrices. Other methods include validated spectrophotometric assays, HPLC methods and ion-selective approaches where fit for purpose. Selection should be based on sensitivity, specificity, throughput and the chemical interferences expected from beetroot pigments, organic acids, chloride, proteins and concentrated soluble solids. Any rapid on-site method intended for batch release should be cross-validated against an appropriate reference procedure on the actual product.

Several seemingly minor laboratory details can change results. Sample holding time, storage temperature, dilution, deproteinization when relevant, filtration membrane interactions, instrument calibration, the distinction between ion and salt mass, and the timing between sampling and preservation all matter. Nitrite is more labile than nitrate in many environments; the two species should not be treated as one undifferentiated “nitrate-related” signal. A sample that continues to undergo microbial transformation after collection can provide an apparently precise but historically inaccurate measurement of the manufacturing lot.

The experimental unit also matters. Five injections of one bottle are analytical replicates, not five production batches. A company establishing supplier reproducibility should sample independent harvests, extraction batches and

industrial lots across relevant seasons. The design should distinguish within-batch heterogeneity from among-batch variation and, where appropriate, combine these sources of uncertainty when setting acceptance criteria.

A useful release panel extends beyond nitrate alone. At a minimum, product-specific assessment should address nitrate, nitrite, pH, titratable acidity, °Brix, microbial indicators and pathogens where relevant, shelf-life conditions, packaging integrity, sensory quality and any legally relevant contaminants. Concentrated preparations may also require evaluation of heavy metals, pesticide residues and other origin-related risks. The purpose is not to create the longest possible certificate of analysis, but to test all variables capable of invalidating the intended chemical dose or product safety.

**Table 2. Industrial analytical identity of a nitrate-containing vegetable ingredient**

| Attribute | Recommended analytical or documentary evidence | Why it matters |
|---|---|---|
| Botanical origin | Species/cultivar, supplier, harvest, agricultural records | Natural nitrate accumulation and co-constituents vary |
| Nitrate ion | Validated ion-specific method; mg $NO_3^-$/kg or per serving | Defines exposure and permits study comparison |
| Nitrite ion | Sensitive ion-specific measurement at release and through shelf life | Detects conversion and potential safety change |
| Matrix and pigments | pH, acidity, °Brix, betalain profile if claimed or critical | Distinguishes dose stability from sensory stability |
| Microbial quality | Product-specific hygiene, pathogen and spoilage controls | Limits post-process ion conversion and deterioration |
| Shelf-life kinetics | Multiple time points, realistic temperature and light challenge | Establishes composition at consumption rather than manufacture only |
| Contaminants | Risk-based pesticide, metals and other relevant assays | Supports overall safety of concentrated inputs |
| Batch reproducibility | Independent harvest and manufacturing batches | Prevents false confidence from analytical replicates |

## 9. Exposure and toxicology: risk cannot be solved by changing vocabulary

A biological pathway capable of producing NO is not evidence that exposure is risk-free. Nitrate and nitrite have long been examined in the context of methaemoglobin formation, especially for infants, and possible formation of N-nitroso compounds under specific chemical conditions. The toxicological relevance of a specific product depends on dose, consumer characteristics, the concentrations of nitrate and nitrite, their conversion, co-exposures and the finished matrix. The term “vegetable-derived” should not be treated as a substitute for an exposure calculation.

In its 2017 re-evaluation, EFSA maintained an acceptable daily intake for nitrate of **3.7 mg/kg body weight per day** and re-established an ADI for nitrite of **0.07 mg/kg body weight per day**. These figures must be interpreted within the scope of the assessments and the totality of dietary exposure. EFSA also reported that food-additive nitrate represented only a relatively small share of overall dietary nitrate exposure, while natural sources and water could contribute substantially. The ADI is a toxicological reference used for assessment of repeated exposure, not a dosing instruction for functional foods and not a guarantee that any exposure below it is effective or risk-free for every person (EFSA ANS Panel, 2017; EFSA, 2017).

The practical dose arithmetic illustrates why unit discipline matters. A beverage containing **400 mg nitrate ion** delivers approximately **6.45 mmol $NO_3^-$**. For a hypothetical 70 kg adult, 400 mg corresponds to **5.7 mg/kg body weight**, numerically above the 3.7 mg/kg/day ADI when considered alone. This does not automatically establish that a single such serving causes harm; neither does a positive clinical trial nullify the need for repeated-exposure and population-specific assessment. Equally, ordinary consumption of vegetables should not be discouraged merely because a high-vegetable diet can exceed a conservative nitrate ADI in some circumstances. EFSA's 2008 risk–benefit evaluation concluded that the benefits of eating vegetables and fruit generally outweighed nitrate-related risks under the assessed dietary conditions.

The risk profile is not uniform across ages. Infants and young children require determined consideration because of developmental physiology, food-category exposure and the possibility of comparatively high intake per kilogram of body weight. Specific nitrate limits apply to certain infant and young-child foods in EU law. They should not be copied indiscriminately into ordinary adult beverages, but a manufacturer should not use adult clinical evidence as a basis for marketing concentrated nitrate preparations to children.

Nitrosation chemistry also deserves careful language. Some N-nitrosamines are genotoxic and carcinogenic, but their presence or formation cannot be inferred directly from nitrate concentration alone. The food environment includes

amines, nitrite, acidity, oxygen conditions and potential inhibitors such as ascorbate. Different manufacturing routes can alter these factors. A justified safety dossier should identify where N-nitroso hazards are plausible rather than claim that every nitrate-rich vegetable creates the same risk as a cured-meat formulation—or that vegetable origin makes such chemistry impossible.

Consumers taking medicines affecting blood pressure or nitric-oxide signalling, and people with specific clinical conditions, are not an appropriate target for unsupported therapeutic positioning. Clinical questions involving medication, hypotension risk or relevant disease require healthcare judgement. An ordinary food product must not be marketed as a substitute for medical management.

## 10. The European legal framework is an architecture of uses, not a single nitrate rule

Three regulatory situations should be addressed separately: naturally present nitrate treated as a contaminant or exposure parameter in specified food categories; nitrate or nitrite deliberately used as an additive for a technological purpose; and the marketing of a food containing nitrate with an associated nutritional or health message. Each situation has a different legal test. A legally acceptable concentration of nitrate in a vegetable does not authorize every claim about its physiological effects, and a permitted additive use of potassium nitrate in a particular cheese category is not a general authorization to fortify a drink for vascular performance.

**10.1 Naturally occurring nitrate and maximum contaminant levels.** Commission Regulation (EU) 2023/915 sets maximum levels for nitrate in selected categories, including spinach, certain lettuces, rocket and baby food or processed cereal-based food intended for infants and young children. The table is differentiated by product, sometimes season, growing conditions and whether the material is fresh or processed. For example, the entry for fresh spinach specifies **3,500 mg $NO_3^-$/kg**, with a particular exception for fresh spinach sent directly in bulk to processing. That number is not a general maximum for any vegetable juice; beetroot concentrate or dietary supplement. For infant and young-child foods, the regulation contains a separate **200 mg $NO_3^-$/kg** entry for the defined category, with a ready-to-use basis. A legal assessment must verify both the category and the relevant footnotes against the consolidated text effective on the date of marketing.

The absence of a specific maximum level for a particular adult vegetable drink must not be misrepresented as a legal invitation to use unlimited nitrate. Regulation (EC) No 178/2002 continues to prohibit placing unsafe foods on the market; Regulation (EC) No 852/2004 requires hygienic production and procedures based on HACCP principles where applicable. Exposure evaluation, supplier control and analytical specifications remain necessary independently of category-specific limits. The regulatory risk may also concern a concentrated extract whose origin or manufacturing history differs materially from conventional food use.

**10.2 Additive identity and the 2025–2026 transition.** Regulation (EC) No 1333/2008 governs food additives, including E 249 and E 250 (nitrites) and E 251 and E 252 (nitrates), within defined food categories and technical conditions. Commission Regulation (EU) **2023/2108** revised maximum permitted levels, purity specifications and related conditions, with application dates that differ across entries, notably in **October 2025 and October 2026**. By November 2026, one should not rely on an outdated table that omits the later transition, nor treat all values as residual finished-product limits: certain provisions specify maximum quantities *added during manufacture*, expressed as nitrate or nitrite ion, with separate residual-monitoring or investigation provisions. The precise regulatory footnotes matter as much as the principal numerical value.

This distinction can affect technological development in cheese and cured foods, but it must not be imported into ordinary beetroot-beverage specifications. If the ingredient is a traditional vegetable used in a beverage for its ordinary food characteristics, the regulatory analysis is not made correct by describing the nitrate ion as an authorized additive. Conversely, if an isolated nitrate salt is deliberately added for a technological purpose, the additive framework must be examined rather than bypassed by appealing to studies of beetroot juice. Actual function, ingredient identity, product category, intended use and labelling determine the route.

**10.3 Novel foods and concentrated materials.** Regulation (EU) 2015/2283 raises questions when a proposed ingredient lacks a significant history of consumption within the Union before 15 May 1997 or meets another relevant definition, including certain altered manufacturing processes that significantly affect composition or structure. Beetroot as a familiar vegetable is not, for that reason alone, proof that every highly purified, engineered or unusually processed nitrate-rich preparation is legally equivalent to conventional beetroot juice. Where doubt exists, the source, process, consumption history, intended uses and Union-list status should be reviewed through an appropriate

documented procedure. Conversely, the term "concentrated" alone does not automatically prove novelty. Classification must be evidence-led.

**10.4 Claims: physiological plausibility is not marketing authorization.** Regulation (EC) No 1924/2006 controls nutrition and health claims and must be read together with the EU register and relevant implementing acts. A clinical study of vascular function does not itself authorize phrases such as "lowers blood pressure", "prevents hypertension", "improves circulation" or "protects the heart" on a consumer food label. The exact authorized claim, substance, food composition, qualifying conditions, target population and permitted wording must be checked individually. A generic reference to beetroot or to endogenous NO formation cannot be assumed to qualify as an authorized statement. Regulation (EU) No 1169/2011 remains relevant to mandatory and voluntary consumer information, including the prohibition of misleading presentation. Therapeutic or disease-treatment assertions may engage restrictions beyond ordinary food-health-claim rules.

**Table 3. Legal decision map for nitrate-containing foods in the European Union**

| Regulatory question | Principal framework | What must be decided | Invalid shortcut |
|---|---|---|---|
| Is nitrate naturally present in a vegetable subject to a maximum level? | Regulation (EU) 2023/915 | Exact food category, stage of marketing, relevant footnotes and concentration | "The spinach value is the legal limit for every juice" |
| Are nitrate/nitrite salts added for a technological purpose? | Regulation (EC) 1333/2008 as amended by 2023/2108 | Additive identity, approved use, category, application date, added amount and relevant residual rules | "An E number allows arbitrary nitrate addition to a beverage" |
| Does an unconventional material require novel-food examination? | Regulation (EU) 2015/2283; Union list 2017/2470 | Exact source, process, compositional change, consumption history and permitted uses | "Any beetroot-derived extract is automatically traditional" |
| Is the finished food safe? | Regulations (EC) 178/2002 and 852/2004 | Total exposure, consumer groups, microbial stability, nitrite and other hazards | "No category-specific nitrate limit means no safety obligation" |
| Is the proposed cardiovascular claim authorized? | Regulation (EC) 1924/2006; EU claims register | Specific approved wording, conditions, ingredient and product | "A randomized trial authorizes a blood-pressure claim" |
| Is consumer information correct? | Regulation (EU) 1169/2011 | Measurable dose, serving, ingredients, non-misleading statements | "Red colour or beetroot content proves a dose of nitrate" |

The entries are a regulatory reasoning framework, not a product-specific authorization opinion.

## 11. A proposed beverage platform: standardization before positioning

Consider a hypothetical industrial customer interested in a 70–100 mL vegetable shot for adult consumers. The customer has seen acute vascular studies using several hundred milligrams of nitrate and proposes reproducing the exposure through beetroot concentrate. The most attractive starting point would be to specify the intended nitrate-ion content in mg per serving and the allowable variability throughout shelf life. The product's legal classification, the intended consumer group and proposed label language must be established before the marketing team commits to a cardiovascular positioning.

In the first experimental stage, two or three raw-material sources should be compared across different harvests. Both nitrate and nitrite should be assayed before formulation. The specification should distinguish concentration measured on a wet or dry basis; the finished beverage should be calculated from independently checked composition rather than from an assumed typical beetroot value. If a supplier claims, for example, a target of 400 mg $NO_3^-$ per serving, a validated assay must establish that the finished shot—not just the starting extract—meets the specification. This is a design example, not an existing INTABIOTECH formula or a recommendation that a daily 400 mg dose is universally safe or legally suitable.

The second stage should evaluate processing. A reference matrix would be fixed for acidity, soluble solids, sweetness, salt profile and stabilizing ingredients. Controlled trials would compare process options with replicate manufactured batches, measuring nitrate/nitrite, colour, oxygen, microbiology and sensory attributes before and after treatment. Thermal history and residence time should be documented. An effective preservation treatment should achieve the required food-safety objectives while maintaining an acceptable dose and shelf-life profile. An observed reduction in

microbial plate counts would not establish that nitrite cannot accumulate later if recontamination or package failure occurs.

The third stage should investigate realistic distribution and consumer use. A sealed sample held under ideal laboratory refrigeration cannot establish the same stability as the beverage in transport, retail handling and in-use storage after opening. Temperature-cycling and light-exposure trials should complement real-time shelf-life measurement; no single accelerated factor should be presumed to predict every chemical and microbial reaction. A separate traceability study should test whether the company can identify and segregate raw-material lots with unusually high or low nitrate concentration before blending.

Only after composition, safety and industrial functionality are established should a human intervention be considered. If the scientific objective is acute vascular physiology, the trial should be prospectively registered, appropriately powered, randomized and controlled, with nitrate-depleted or otherwise carefully matched comparator where feasible, and with prespecified outcomes. Oral antiseptic exposure, recent dietary nitrate, medication, age, sex, baseline blood pressure and physical activity should be treated as potential sources of variability. A trial should measure the finished product used by participants, not an abstract ingredient specification established months earlier.

**A crucial commercial limitation remains:** *a positive proprietary intervention would strengthen the scientific dossier, but it would not by itself confer authorization for a health claim in the EU. Claim strategy must be designed in parallel with research, rather than appended after the results are seen.*

## 12. Experimental design: disentangling nitrate, beetroot matrix and microbiome effects

A sophisticated clinical or translational programme should address what many short beetroot studies cannot: source equivalence, matrix contribution and variation in entero-salivary conversion. For example, a study could compare a standardized nitrate-rich beetroot preparation with a nitrate-depleted but otherwise closely matched beetroot matrix and an alternative nitrate-containing preparation, subject to ethical, scientific and legal feasibility. Such a design would require care because nitrate depletion can alter matrix chemistry, taste and other constituents; a comparator that is analytically “matched” for one variable may be different for others.

A two-factor design could investigate nitrate dose and the matrix in which it is consumed. The endpoints should be selected to match the hypothesis. Salivary and plasma nitrate/nitrite could establish exposure and pathway engagement; ambulatory blood pressure or endothelial-function testing could evaluate a physiological endpoint; gastrointestinal tolerance and adverse events would address safety; and defined oral-microbiome functional assays might explain response variation. None should be substituted for the other. An observed salivary-nitrite rise is not the primary outcome if the commercial proposition is a vascular benefit.

Repeated-measures designs can increase statistical efficiency but also create interpretive risks. Washout periods should be justified. Treatment-order effects and baseline diet need consideration. Multiple related outcome measures require a prespecified statistical hierarchy to avoid selective reporting. The analytical batches used during the trial should be retained where practicable for independent composition verification. Human outcomes should be interpreted using effect size, confidence intervals and clinical relevance rather than a binary statistically significant/not-significant classification.

The microbiome component should avoid an unnecessary claim to broad profiling sophistication. Metagenomic abundance, nitrate-reductase gene content and actual in-vivo nitrate-reduction activity answer different questions. If a model predicts responders from oral bacterial genera, it must be evaluated on independent participants, not only through cross-validation in the same small cohort. In a manufacturing-oriented programme, it may be more cost-effective to record oral-hygiene status and use a targeted functional assay than to undertake an expansive, underpowered omics study.

## 13. Safety surveillance and consumer communication

A concentrated vegetable product should be designed for the consumers likely to use it, not the population for which the most favourable trial was conducted. Sports-nutrition users may combine shots with other nitrate-rich products; people using cardiovascular medicines may have different baseline blood pressure; and children may be inadvertently

exposed through household use. Cumulative dietary exposure and reasonably foreseeable misuse matter even when the product is categorized as an ordinary food.

The manufacturing system should also address the difference between intentional fortification and natural variation. A label that quantifies nitrate per serving creates a need for substantiation at consumption, including within-batch homogeneity and a justified shelf-life tolerance. If the concentration is given as a range, that range must reflect actual measured variation and the overall presentation must not mislead. Claims of “natural nitric oxide” are chemically imprecise: a bottle ordinarily contains nitrate-bearing ingredients, not a stable, physiologically relevant dose of free NO. Terminology must reflect the analyte present.

Safety should not be reduced to a single nitrate cut-off. If nitrite accumulates under abuse conditions, if microbial counts rise, or if taste deteriorates before the declared shelf life, the product has failed a relevant requirement regardless of its nominal nitrate dose. An internal action limit should be connected to analytical uncertainty and a documented corrective-action plan. For more concentrated or unfamiliar products, the risk assessor should consider whether additional evidence on methaemoglobin-related susceptibility, nitrosation conditions or co-ingredient exposure is warranted.

Communications should also resist the opposite exaggeration: natural vegetable nitrate should not be portrayed as an equivalent hazard to every additive-nitrite application in processed foods. Matrix, precursor compounds, processing and overall dietary pattern matter. Distinguishing risks does not require dismissing them. The strongest scientific message is that benefits and hazards must be examined within the same specified exposure pathway.

## 14. Data science, traceability and the boundaries of prediction

Nitrate-rich vegetable products are well suited to data-driven process development because raw-material concentration, weather, harvest, processing conditions and storage chemistry generate substantial variance. A multivariate model could investigate how season, cultivar, field nitrogen practices, pre-processing delay, pH, pasteurization conditions and packaging predict the release concentration and shelf-life evolution of nitrate and nitrite. Such a model would have commercial value if it reduced out-of-specification lots or improved targeting of analytical resources.

However, cross-validation conducted on many measurements from one harvest may exaggerate transferability. A reliable approach should separate training and validation by field, harvest date, supplier and independent factory batch. Method changes must be recorded. The model should include physical and legal constraints: no predicted formulation should bypass a product-specific contaminant limit, an inapplicable additive authorization or an unacceptable microbiological result merely because it is economically attractive.

The distinction between a predictive quality model and a mechanistic model is also important. A classifier that predicts nitrate concentration from visible colour may exploit correlations in a specific cultivar while failing after a supplier change. It does not thereby discover nitrate chemistry. Independent ion-specific analysis remains necessary for release verification unless a fully validated alternative approach satisfies the decision. An AI-generated confidence interval is not a substitute for laboratory uncertainty or experimental replication.

An industrial digital dossier should link each finished lot to raw-material origin, validated ion assays, process parameters, food-safety verification, packaging, product complaints and real-time stability outcomes. Such traceability is especially valuable when the formulation depends on a constituent whose concentration changes markedly with seasonal agriculture. The strategic asset is a supply platform that can deliver a consistent, lawful product across variable harvests, not the possession of a visually attractive analytical dashboard.

## 15. Economic feasibility: the active unit must be the saleable serving

Nitrate standardization creates costs beyond the purchase price of beetroot solids. Suppliers may need to segregate high- and low-nitrate harvests, blend raw materials, stabilize extracts, repeat analytical assays, manage rejected lots and use protective packaging. Concentration may reduce transport volume but increase processing energy, viscosity or flavour-management requirements. An ingredient whose nitrate content is high, but whose flavour is unacceptable can be economically inferior to a lower-titer preparation that performs reliably in a finished product.

Procurement should therefore compare **cost per compliant serving of nitrate-containing finished food**, not only kilograms of beetroot powder. A realistic model incorporates laboratory verification, losses at each unit operation,

seasonal variability, shelf-life wastage, packaging, logistical controls and regulatory maintenance. The lowest quoted price per kilogram can conceal the highest overall cost if substantial blending or rework is required.

For INTABIOTECH, the potential role is an ingredient-engineering and evidence-development platform: sourcing qualified botanical ingredients, designing formulations, coordinating analytical studies, validating manufacturing conditions and assisting clients with legally accurate product dossiers. This is an industrial research opportunity, not a claim that the company has already demonstrated cardiovascular efficacy or manufactures a clinically validated nitrate product. A development decision should follow proof of market fit and lawful positioning rather than precede those requirements with an unsupported health claim.

## 16. A minimum evidence package for responsible commercialization

A concise industrial dossier can still be scientifically demanding. It should identify the source and process, describe the chemical species and dose, quantify uncertainty, establish safety through the intended distribution chain, and specify which statements may lawfully accompany the product. The most important design decision is to prevent one type of evidence from silently standing in for another.

**Table 4. Stage-gated evidence package for an EU nitrate-containing beverage project**

| Gate | Evidence required | Decision to be made |
|---|---|---|
| I — Intended identity | Botanical and process description; proposed food category; legal screening | Is the proposed ingredient and use legally plausible? |
| II — Dose identity | Nitrate- and nitrite-ion assays, analytical units, batch variation | Can the product deliver a reproducible composition? |
| III — Manufacturing | Process validation, hygienic controls, holding times, oxygen and pH | Is dose integrity compatible with food safety? |
| IV — Shelf life | Real-time nitrate/nitrite, microbiology, pigments, sensory and package testing | Does the product remain acceptable until consumption? |
| V — Exposure | Serving, consumption frequency, user groups, cumulative diet and toxicology | Is the intended use supportable within a risk assessment? |
| VI — Human evidence | Properly controlled intervention with prespecified physiological endpoints, if needed | What effect, if any, is demonstrated for the exact formulation? |
| VII — Regulatory communication | EU food category, contaminant/additive/novel-food status and exact claims screening | Can the finished food and its message lawfully enter the market? |
| VIII — Commercial scale | Replicate batches, supplier variability, cost per compliant serving, traceability | Does the technology create durable industrial value? |

## 17. Discussion: the nitrate paradox is a useful model for precision food science

The scientific rehabilitation of dietary nitrate as a possible participant in NO biology has been important. It demonstrates that substances historically considered only in the context of exposure and toxicology may also participate in physiological signalling. Yet the existence of this pathway does not reverse the ordinary scientific requirements for nutrition research. It instead makes the evidence chain more intricate. A food must supply a measured chemical exposure; an individual must convert that exposure through a variable microbial and host pathway; a physiological endpoint must change in a meaningful manner; and any proposed commercial communication must have a lawful basis.

The latest human studies are notable precisely because their findings differ. McLellan and colleagues observed distinct dose-related responses across arterial stiffness, endothelial function and central blood pressure rather than a universal graded effect. Other studies have used larger nitrate doses, different beetroot preparations and populations with metabolic or cardiovascular conditions. Mechanistic oral-microbiome work strengthens causal plausibility but does not settle long-term efficacy. Small pilot trials cannot be converted into disease-prevention claims by the rhetorical accumulation of positive biomarkers.

In parallel, the technology of the food can undermine the clinical premise. Agricultural variability, microbial nitrate reduction during storage, nitrite formation, oxygen exposure and the presence of pigments or co-extracted phytochemicals mean that “beetroot juice” is not a standardized intervention unless it is made one. An ingredient supplier who cannot quantify nitrate ion, nitrite ion and finished-product variability cannot credibly argue that its product reproduces a specified clinical exposure.

European law adds a necessary layer of discipline. Contaminant rules, additive authorizations, novel-food provisions and health claims address different questions. The updated additive limits under Regulation 2023/2108 should not be read as general permissions for nutritional nitrate fortification. Nitrate maxima in specified leafy vegetables should not be presented as universal concentration caps for all beetroot preparations. Nor does a mechanistically coherent acute study create a market authorization for cardiovascular claims. This architecture may initially appear inconvenient, but it protects responsible innovation from being confused with regulatory arbitrage.

The strongest commercial opportunity is therefore neither a universal "NO-boosting" ingredient nor the simplistic equation that higher nitrate content means better nutrition. It is the ability to produce a stable, characterized, legally positioned botanical product whose hypothesized physiological action can be tested without obscuring safety, variability or limitations. The discipline required to say exactly what is in the product is inseparable from the discipline required to say what it does.

## 18. Conclusions

Dietary nitrate provides an unusually revealing case study at the intersection of molecular nutrition, microbiology, processing technology, clinical physiology and food law. The nitrate–nitrite–NO pathway is biologically plausible and supported by controlled human investigations, but the translation from intake to meaningful vascular outcome is neither linear nor universal. The oral microbiome contributes to the pathway, yet its functional capacity cannot be reduced to a list of bacterial names. Vegetable-matrix composition, manufacturing and storage determine whether the commercial exposure resembles the intervention investigated in research.

A defensible industrial approach requires independent verification of nitrate and nitrite, control of source and batch variability, realistic shelf-life testing, proportionate toxicological assessment and careful separation of natural content from additive use. European rules for selected vegetable nitrate maxima, additive nitrites and nitrates, novel materials, mandatory information and health claims must be applied according to their respective purposes. Clinical evidence should inform research strategy without being mistaken for permission to market a cardiovascular treatment.

For an ingredient company, the next meaningful innovation is not a stronger adjective for beetroot. It is an evidence-controlled, reproducible and lawful food system whose chemical composition, microbial stability, human-response hypothesis and economic feasibility can each withstand independent examination.

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**Editorial note.** This document is an interdisciplinary critical review and industrial research framework; it does not report new clinical findings or trials carried out by INTABIOTECH. Proposed formulation examples and test designs are illustrative. European rules and clinical studies should be rechecked against the legally consolidated text and primary publications applicable to the intended ingredient and market before commercialization. Bibliographic entries lacking full publisher metadata have been intentionally identified without invented author lists or pagination.

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