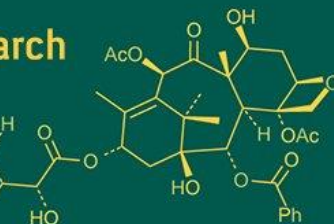
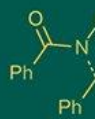


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Designer eggs as functional foods by nutritional enhancement for health benefits

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Abstract

Eggs have long been considered one of nature's most nutritionally complete foods, yet the conventional table egg shaped by decades of production systems optimized for output quantity rather than output quality falls considerably short of its nutritional potential. Designer eggs, produced by strategically manipulating laying hen nutrition, management practices and breed selection, represent a scientifically grounded approach to transforming this everyday staple into a targeted functional food. This review synthesizes evidence published between 2017 and 2025 on the major strategies employed to enhance the nutritional value of table eggs, encompassing enrichment with long-chain omega-3 polyunsaturated fatty acids (n-3 LC-PUFA), selenium, zinc, iodine, vitamins D, E, A and B12, as well as xanthophyll carotenoids including lutein and zeaxanthin. The mechanisms by which targeted dietary supplementation of the laying hen translates into measurable yolk and albumen enrichment are examined in depth, alongside dose-response relationships, transfer efficiencies, bioavailability considerations and sensory quality trade-offs that govern practical application. Clinical evidence is evaluated across cardiovascular lipid profiles, cognitive function, bone mineral density, thyroid metabolism and ocular health endpoints. The review critically addresses common misconceptions particularly the persistent conflation of egg cholesterol content with cardiovascular risk and contrasts these with the weight of current epidemiological and mechanistic evidence. Contraindications, including risks associated with selenium toxicity at supratherapeutic intakes, excessive omega-3 consumption in anticoagulant-dependent individuals, iodine sensitivity in thyroid disease and vitamin D hypervitaminosis, are discussed within a proportionate, public-health-oriented framework. Emerging directions including CRISPR-assisted metabolic enhancement, microbiome-mediated biofortification and precision nutrition applications are evaluated for near-term feasibility. Designer eggs are positioned not as a replacement for dietary diversity, but as a practical, cost-effective and high-compliance vehicle for targeted micronutrient delivery in populations where supplementation adherence is chronically low.

Keywords: Functional food, omega-3 fatty acid enrichment, biofortification, laying hen nutrition, nutraceutical eggs

1. Introduction

The egg occupies a singular position in human nutrition: simultaneously one of the world's most consumed animal-source foods and one of the most nutritionally debated. Global egg production exceeded 85 million metric tonnes in 2023, with per capita consumption rising consistently across low-and middle-income countries driven by economic development and urbanization (Food and Agriculture Organization [FAO], 2023) ^[13]. Within this landscape of scale, even modest improvements to the nutritional profile of the table egg carry transformative public health implications. The concept of the designer egg an egg whose composition has been deliberately tailored through hen nutrition, genetics, or management emerged from this recognition and has since matured into a sophisticated sub-discipline of functional food science (Cherian, 2022) ^[6].

Functional foods are broadly defined as foods that, beyond meeting basic nutritional requirements, confer measurable physiological or health benefits when consumed as part of a habitual diet (Granato *et al.*, 2020) ^[15]. Eggs are naturally rich in high-biological-value protein, choline, fat-soluble vitamins, retinol and antioxidant carotenoids and yet the modern commercial egg is simultaneously a product of narrow-spectrum feeding regimes that constrain its nutritional ceiling.

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Commercial laying hens are typically maintained on corn-soybean meal diets formulated to maximize egg production efficiency rather than yolk or albumen quality. The consequence is an egg product characteristically depleted in omega-3 polyunsaturated fatty acids (PUFA), selenium, iodine and vitamins D and E relative to eggs produced by nutritionally supplemented or pasture-raised hens (Karsten *et al.*, 2019; Leeson & Summers, 2017) ^[20, 23].

Three independent nutritional trends have converged to make designer eggs commercially and clinically relevant. First, population-level omega-3 fatty acid deficiency reflected in an aberrantly elevated omega-6:omega-3 ratio in Western dietary patterns is associated with increased inflammatory burden, cardiovascular disease risk and suboptimal neurodevelopmental outcomes (Simopoulos, 2020) ^[34]. Second, vitamin D insufficiency is estimated to affect over one billion people globally, a consequence of indoor lifestyles, sun avoidance behavior and the limited natural food sources of this nutrient (Holick *et al.*, 2022) ^[18]. Third, selenium status is geographically determined by soil selenium concentrations and large swathes of Europe, Sub-Saharan Africa and parts of Asia remain in a state of subclinical selenium deficiency that impairs selenoprotein-mediated antioxidant protection and immune surveillance (Surai & Fisinin, 2021) ^[38]. Designer eggs address each of these gaps through a single, culturally embedded, affordable food vehicle. In Europe, omega-3-enriched eggs now constitute a meaningful share of the premium egg retail segment, while selenium-enriched and vitamin D-fortified variants are gaining traction in North American, Japanese and Australian markets (Mintel, 2023) ^[27]. This commercial momentum has generated a growing body of scientific literature evaluating both the efficacy of enrichment strategies and their clinical impact on human health biomarkers literature that this review systematically synthesizes and critically evaluates.

An important secondary objective of this review is to address the persistent and sometimes harmful misinformation surrounding egg consumption, particularly the conflation of dietary cholesterol with cardiovascular risk. This conflation rooted in mid-twentieth century dietary science has caused egg consumption to be inappropriately

restricted in populations for whom eggs represent a cost-effective and nutritionally significant dietary staple (Fernandez & Calle, 2021; Godos *et al.*, 2021) ^[11, 14]. The evidence reviewed here situates the egg and its designer variants, within an accurate and contemporary nutritional risk-benefit framework.

2. Nutritional Composition of the Conventional Commercial Egg

Before exploring how eggs can be improved, it is necessary to appreciate what they already provide and where their nutritional limitations lie. A standard large chicken egg (approximately 50 g, with yolk accounting for 32% and albumen for 58% of edible weight) delivers roughly 78 kilocalories, 6.3 g of high-biological-value protein, 5.3 g of total lipid, 212 mg of cholesterol (concentrated almost entirely in the yolk) and meaningful quantities of choline (~147 mg), riboflavin, retinol, selenium and the xanthophyll carotenoids lutein and zeaxanthin (USDA FoodData Central, 2023) ^[42].

The yolk houses the majority of fat-soluble nutrients vitamins A, D, E and K, carotenoids, choline and most of the lipid fraction while the albumen is predominantly protein: ovalbumin (~54%), ovotransferrin (~12%), ovomucin (~3.5%) and lysozyme (~3.5%), among others functionally significant proteins (Mine *et al.*, 2022) ^[26]. The fatty acid profile of the conventional commercial egg yolk is characterized by a high omega-6 to omega-3 ratio, typically ranging from 15:1 to 20:1, far removed from the 4:1 or lower ratio associated with reduced chronic disease risk in epidemiological literature (Simopoulos, 2020) ^[34]. This lipid imbalance is the primary target of the most commercially developed designer egg intervention omega-3 enrichment and reflects the almost exclusive reliance of commercial hen diets on corn and soybean oil as fat sources, both of which are linoleic acid (omega-6)-dominant.

Table 1 presents a comparative overview of macronutrient and micronutrient composition across conventional eggs and major designer egg variants, illustrating the magnitude of compositional differences achievable through targeted intervention.

Table 1: Comparative nutritional composition of a conventional commercial egg versus omega-3 enriched and multi-nutrient designer egg variants per large egg (~50 g). Values are approximate ranges derived from published literature.

Nutrient (per egg)	Conventional Egg	Omega-3 Enriched	Multi-Nutrient Designer Egg
Energy (kcal)	~78	~78	~80
Protein (g)	6.3	6.3	6.4
Total Fat (g)	5.3	5.4	5.5
Cholesterol (mg)	212	200-215	195-215
DHA (mg)	30-50	200-400	200-450
EPA (mg)	5-10	20-60	20-80
ALA (mg)	20-30	150-400	150-400
Selenium (µg)	15-18	15-18	40-80
Iodine (µg)	25-35	25-35	100-150
Vitamin D (µg)	1-2	1-2	15-40
Vitamin E (mg)	0.5-1.0	2-5	8-12
Lutein + Zeaxanthin (µg)	250-300	250-300	800-2500
Vitamin B12 (µg)	0.6	0.6	0.8-1.0
Choline (mg)	~147	~147	~150

3. Fatty Acid Enrichment

3.1 Rationale and Epidemiological Context

Omega-3 polyunsaturated fatty acids principally alpha-linolenic acid (ALA; 18:3n-3), eicosapentaenoic acid (EPA;

20:5n-3) and docosahexaenoic acid (DHA; 22:6n-3) are implicated in a broad spectrum of physiological processes, including the modulation of pro-and anti-inflammatory eicosanoid pathways, neuronal membrane fluidity, retinal

photoreceptor function and cardiovascular lipid metabolism (Calder, 2020) ^[5]. DHA is the structurally dominant fatty acid in the human brain (representing approximately 10-15% of total brain fatty acids) and the retinal photoreceptor outer segment membranes, making adequate supply critical across the lifespan but particularly during fetal development and early infancy (Koletzko *et al.*, 2019) ^[21].

The landmark REDUCE-IT trial a double-blind, placebo-controlled RCT enrolling 8,179 statin-treated patients demonstrated that icosapentaenoic acid ethyl ester supplementation (4 g/day) reduced major adverse cardiovascular events by 25% versus mineral oil placebo, confirming the clinical significance of elevated omega-3 status in high-risk populations (Bhatt *et al.*, 2019) ^[1]. While designer eggs deliver omega-3 quantities below pharmacological thresholds, their role in improving population-level omega-3 status particularly among the many individuals who do not consume oily fish, the conventional dominant dietary source should not be dismissed as trivial. The cumulative effect of modest enrichment across a large population dietary pattern represents meaningful public health opportunity (Cherian, 2022) ^[6].

3.2 Dietary Strategies for Enrichment

The most effective and commercially scalable strategies for omega-3 enrichment involve the targeted manipulation of the laying hen's diet. The primary substrate options, with their respective strengths and limitations, are summarized in Table 2 and discussed below.

Flaxseed (linseed) is the most widely used commercial vehicle for omega-3 enrichment, primarily because of its cost-effectiveness and high ALA content (approximately 57% of total fatty acids). Dietary inclusion at 10-15% substantially increases yolk ALA content but achieves limited DHA deposition, a consequence of the hen's

inherently low hepatic Δ -6 desaturase activity the rate-limiting enzyme in the ALA-to-DHA bioconversion pathway. In practice, approximately 5-10% of dietary ALA is elongated to EPA and DHA in the hen (Milinsk *et al.*, 2022) ^[25]. For ALA itself, however, flaxseed-enriched eggs may offer modest benefit in populations with chronically low ALA intake.

Microalgae particularly DHA-rich species including *Schizochytrium limacinum*, *Thraustochytrid* sp. and *Nannochloropsis oceanica* represent the most effective strategy for increasing yolk DHA content. Algal DHA supplementation at 0.5-1.5% dietary inclusion consistently elevates yolk DHA from conventional values of 30-50 mg to 200-450 mg per egg, without the fishy off-flavor associated with fish oil at equivalent DHA doses (Lemahieu *et al.*, 2019; Xiao *et al.*, 2021) ^[22, 46]. Microalgae represent a fully plant-based, sustainable DHA source that also avoids the pollutant concerns (dioxins, PCBs) occasionally raised for fish oil products.

Fish oil remains highly effective for simultaneous EPA and DHA deposition, but sensory quality deteriorates at dietary inclusion rates exceeding 2-3% due to PUFA peroxidation and the accumulation of volatile aldehydes and secondary lipid oxidation products in the yolk (Van Hecke *et al.*, 2018) ^[44]. Co-supplementation with natural antioxidants α -tocopherol, rosemary extract (*Rosmarinus officinalis*), or green tea polyphenols significantly attenuates this problem and extends shelf-life stability in enriched eggs (Lopez-Bote *et al.*, 2019) ^[24].

Chia seed (*Salvia hispanica*) is emerging as a practical ALA source with favorable palatability and unlike flaxseed, it does not require grinding for optimal fatty acid availability. Inclusion rates of 5-10% in layer diets yield enriched eggs comparable to flaxseed-supplemented eggs without negative effects on egg production performance (Peiretti *et al.*, 2022) ^[30].

Table 2: Fatty acid enrichment strategies for laying hens: dietary substrate, inclusion rate, yolk DHA deposition and sensory impact.

Dietary Source	Inclusion Rate	Yolk DHA (mg)	Yolk ALA (mg)	Sensory Impact
Control (no supplement)		30-50	20-30	None
Flaxseed/Linseed	10-15% diet	60-100	250-500	Minimal
Chia Seed	5-10% diet	50-90	200-450	Minimal
Fish Oil	1-3% diet	130-280		Fishy (>2%)
Microalgae (DHA-rich)	0.5-1.5% diet	200-450		Minimal to none
Algae + Vit. E co-supp.	0.5-1.5% + 200 mg/kg	200-420		None

3.3 Transfer Efficiency and Plateau Kinetics

The transfer of dietary fatty acids into egg yolk is not linear. Yolk fatty acid composition reaches a compositional plateau after approximately 14-21 days of supplemented feeding, governed by the saturation of yolk phospholipid remodeling pathways. The efficiency of DHA deposition from microalgae is considerably higher than from ALA precursors, yielding a 3-5-fold greater DHA enrichment per unit of dietary fatty acid consumed (Cherian, 2022) ^[6]. Once supplementation is discontinued, yolk DHA returns to baseline within 10-14 days, indicating that ongoing dietary enrichment is required for sustained product quality.

3.4 Human Clinical Evidence

Randomized controlled trials evaluating omega-3-enriched egg consumption in humans have yielded evidence of modest but clinically relevant effects on cardiovascular risk

biomarkers. In a 12-week, parallel-group RCT, daily consumption of two algal-DHA-enriched eggs (providing approximately 300 mg DHA/day) reduced fasting serum triglycerides by 14% and significantly elevated HDL-cholesterol compared with conventional egg consumption in hyperlipidemic adults, with no significant change in LDL-cholesterol (Dawczynski *et al.*, 2018) ^[7]. A systematic review of nine RCTs using omega-3 enriched eggs concluded that consumption reliably increases plasma phospholipid DHA concentrations in healthy adults, with effect sizes proportional to enrichment level and baseline DHA status (Tan *et al.*, 2021) ^[40].

3.5 Conjugated Linoleic Acid (CLA) Enrichment

Beyond omega-3 PUFA, conjugated linoleic acid (CLA) a group of geometric and positional isomers of linoleic acid produced by ruminal biohydrogenation in ruminants has

received attention as a secondary designer egg target. Eggs from pasture-raised hens naturally contain 2-3 times higher CLA concentrations than caged-hen eggs, reflecting greater access to insects and green plant material (Karsten *et al.*, 2019) ^[20]. CLA has demonstrated anti-carcinogenic, anti-atherogenic and adipogenesis-inhibiting properties in animal models, though translational evidence in human trials remains heterogeneous, with effects strongly dependent on isomer ratio, dose and study duration (Trigueros *et al.*, 2020) ^[41]. Direct dietary supplementation of laying hens with rumen-protected CLA can further elevate yolk CLA content beyond what free-range access alone achieves, offering a controlled enrichment strategy for commercial production settings.

4. Mineral Enrichment

4.1 Selenium

Selenium is an essential trace element whose biological roles are mediated almost entirely through the family of selenoproteins over 25 identified in humans including glutathione peroxidases (GPx1-4), thioredoxin reductases (TrxR1-3) and selenoprotein P (SELENOP), the primary hepatic selenium exporter responsible for delivering selenium to the brain, testes and thyroid (Surai & Fisinin, 2021) ^[38]. These selenoproteins collectively regulate cellular redox homeostasis, immune competence, thyroid hormone metabolism and reproductive function. Selenium deficiency is causally linked to Keshan disease (endemic cardiomyopathy in low-selenium regions of China), Kashin-Beck osteoarthropathy, impaired thyroid function and increased susceptibility to viral mutagenesis.

Hen supplementation with either inorganic sodium selenite or organic selenomethionine is among the most established and commercially implemented designer egg interventions. The critical distinction between these two forms lies in transfer efficiency: organic selenium (selenomethionine and selenium-enriched yeast) deposits into the yolk at approximately twice the efficiency of inorganic selenite, yielding eggs containing 40-80 µg selenium per egg compared with 15-18 µg in unsupplemented controls, without approaching the tolerable upper intake level (UL) of 400 µg/day (Surai & Fisinin, 2021; Skřivan *et al.*, 2020) ^[38, 35]. Additionally, selenium deposited as selenomethionine in the yolk protein matrix exhibits superior bioavailability (~90% absorption efficiency) relative to inorganic selenium (~50-60%). A 12-week randomized controlled trial conducted in selenium-deficient adult volunteers demonstrated that daily consumption of two selenium-enriched eggs (delivering approximately 75-80 µg Se/day as selenomethionine) significantly increased plasma SELENOP concentrations and erythrocyte GPx1 activity functional biomarkers of selenoprotein adequacy compared with conventional egg consumption, without exceeding the UL in any participant (Nagy *et al.*, 2019) ^[28]. These findings support the practical utility of selenium-enriched eggs as a food-based intervention in selenium-deficient geographic regions.

4.2 Zinc

Zinc is indispensable for immune cell development, wound healing, protein synthesis and the catalytic activity of more than 300 metalloenzymes. Dietary zinc bioavailability is substantially lower from plant sources due to phytate binding, making animal-source zinc including egg yolk zinc

a high-priority dietary source for populations with limited red meat intake. Hen supplementation with organic zinc chelates (zinc methionine, zinc propionate) increases yolk zinc deposition by 25-40% relative to inorganic zinc sulfate supplementation, consistent with the superior absorption and transport efficiency of amino acid-chelated mineral forms (Świątkiewicz *et al.*, 2021) ^[39]. A well-enriched designer egg can deliver 1.5-2.0 mg zinc up to 18% of the adult male recommended dietary allowance of 11 mg/day in a highly bioavailable form.

4.3 Iodine

Iodine deficiency remains the leading cause of preventable cognitive impairment and goiter globally, affecting an estimated 1.88 billion people in regions where soil iodine is low and dietary diversity is insufficient to compensate (Haldimann *et al.*, 2022) ^[17]. The conventional commercial egg is already a naturally moderate iodine source, providing 25-35 µg per egg, but this can be dramatically elevated through hen supplementation with potassium iodide or calcium iodate at dietary concentrations of 5-20 mg/kg. Iodine-enriched eggs containing 100-150 µg per egg have been produced under controlled research conditions and in commercial pilot settings, allowing a single egg to meet or substantially exceed the adult daily requirement of 150 µg and to contribute meaningfully toward the elevated requirements of pregnant women (250 µg/day) and lactating mothers (290 µg/day) (Haldimann *et al.*, 2022) ^[17]. This enrichment potential is of particular relevance in mountainous inland regions including parts of South Asia, Sub-Saharan Africa and Central Europe where seafood intake is negligible and salt iodization programs may be inconsistently implemented.

4.4 Calcium, Iron and Phosphorus

While the eggshell not the edible portion is the primary calcium repository (containing over 90% of the egg's total calcium as calcite), the yolk contains approximately 22 mg calcium per egg in a moderately bioavailable form. Iron enrichment of eggs presents a specific challenge: dietary iron supplementation to laying hens promotes yolk lipid peroxidation through Fenton chemistry, compromising sensory quality and oxidative stability unless concurrent antioxidant co-supplementation (vitamin E, selenium, rosemary extract) is employed to neutralize free radical initiation (Pisarski *et al.*, 2020) ^[32]. Phosphorus, present primarily as phytic acid-bound phosphorus in conventional plant-based hen diets, is bioavailable in the yolk as organic phospholipid phosphorus contributing to choline metabolism and membrane integrity without presenting enrichment challenges comparable to those of iron or selenium.

5. Vitamin Enrichment

5.1 Vitamin D

Vitamin D insufficiency is one of the most prevalent nutritional deficiencies in the modern world, affecting an estimated 40-50% of adults in Europe, North America and the Middle East and disproportionately impacting individuals with limited sun exposure, darker skin pigmentation, obesity and advanced age (Holick *et al.*, 2022) ^[18]. Its physiological consequences extend well beyond classical rickets and osteomalacia to encompass impaired innate and adaptive immune function, increased

susceptibility to respiratory infections, associations with autoimmune disease onset and emerging metabolic and cardiovascular risk markers. Conventional eggs provide approximately 1-2 µg vitamin D3 per egg, positioning them as a minor but meaningful dietary source particularly relevant given that very few foods naturally contain significant vitamin D.

Hen supplementation with vitamin D3 (cholecalciferol) or its more biologically potent metabolite, 25-hydroxyvitamin D3 [25(OH)D3], dramatically increases yolk vitamin D content. At supplemental doses of 2,000-5,000 IU vitamin D3 per kg diet, yolk D3 content rises to 8-20 µg per egg; at equivalent molar doses of 25(OH)D3, yolk deposition reaches 15-40 µg per egg (Browning & Cowieson, 2020) [3]. The clinical significance of the form matters: 25(OH)D3 in the yolk matrix exhibits approximately 5-fold greater bioavailability than native D3 in human pharmacokinetic studies, a consequence of its ability to bypass the rate-limiting hepatic 25-hydroxylation step and enter the systemic vitamin D economy directly (Grundmann *et al.*, 2021) [16].

In a 26-week double-blind RCT enrolling vitamin D-insufficient adults (baseline serum 25(OH)D < 50 nmol/L), daily consumption of one vitamin D3-enriched egg (containing 25 µg D3) raised serum 25(OH)D3 concentrations by a mean of 14 nmol/L comparable to equivalent-dose oral D3 supplementation and sufficient to shift a meaningful proportion of participants from insufficiency toward adequacy (Grundmann *et al.*, 2021) [16]. UV-B irradiation of eggs post-lay represents an alternative non-supplemental enrichment strategy, generating vitamin D3 and vitamin D2 in the yolk surface; however, dose standardization and industrial scalability remain barriers to commercial implementation.

5.2 Vitamin E

Vitamin E (α -tocopherol) is the predominant lipid-soluble chain-breaking antioxidant in biological membranes, protecting polyunsaturated fatty acid side chains from propagating peroxidation cascades initiated by reactive oxygen species. The biological relevance of vitamin E to designer eggs is twofold: as a consumer-directed health benefit and as a product quality preservative. The omega-3 enrichment strategies that increase yolk PUFA content simultaneously increase the oxidative substrate load making concurrent vitamin E enrichment both scientifically logical and technologically necessary for product stability during extended refrigerated storage.

Hen dietary supplementation with α -tocopherol acetate at 150-200 mg/kg diet approximately 5-10 times above NRC minimum recommendations elevates yolk α -tocopherol content from approximately 0.5-1.0 mg in conventional eggs to over 8-12 mg per egg, representing 53-80% of the adult adequate intake (AI) of 15 mg/day (Surai, 2020) [37]. Oxidative stability of omega-3-enriched eggs co-supplemented with vitamin E is significantly superior to eggs enriched with omega-3 alone, with thiobarbituric acid-reactive substance (TBARS) values remaining within acceptable limits through 21 days of refrigerated storage (Lopez-Bote *et al.*, 2019) [24]. Clinical evidence suggests that regular consumption of vitamin E-enriched eggs may modestly attenuate systemic markers of oxidative stress 8-isoprostane, malondialdehyde in elderly populations whose antioxidant defense capacity is age-diminished, though

effect magnitudes are smaller than pharmacological vitamin E supplementation.

5.3 Vitamin B12

Cobalamin (vitamin B12) deficiency is disproportionately prevalent among older adults (due to declining gastric acid and intrinsic factor secretion), strict vegetarians and vegans, individuals with inflammatory bowel disease and populations in low-and middle-income countries with limited animal-product access. Inadequate B12 status impairs one-carbon metabolism, DNA methylation, myelin synthesis and erythropoiesis, with neurological consequences that can be irreversible if left untreated. The conventional egg provides approximately 0.6 µg vitamin B12 per egg one quarter of the adult RDA of 2.4 µg primarily in the yolk as hydroxocobalamin and adenosylcobalamin, both highly bioavailable forms (Bjelakovic *et al.*, 2023) [2]. While B12 enrichment of eggs through hen dietary supplementation is less intensively studied than fat-soluble vitamin enrichment, evidence suggests that high-dose dietary or parenteral cobalamin supplementation in hens can increase egg B12 content by 20-40% and that egg-matrix B12 is absorbed with efficiency comparable to other food-form cobalamins (Bjelakovic *et al.*, 2023) [2].

5.4 Folate

Folate is indispensable for de novo nucleotide synthesis and one-carbon transfer reactions essential to DNA replication, repair and methylation. Neural tube defects, caused by periconceptional folate deficiency, remain a preventable global public health burden. Egg yolk naturally contains approximately 22-28 µg of folate per egg, primarily as 5-methyltetrahydrofolate (5-MTHF), the bioactive form directly usable in the methionine cycle. The food matrix of the yolk rich in folate-binding proteins retains folate during cooking more effectively than many vegetable sources and bioavailability of egg yolk folate appears favorable relative to synthetic folic acid in fortified grain products (Stover & Field, 2018) [36]. Hen dietary supplementation with folic acid modestly increases yolk folate deposition, supporting an argument for eggs as a folate vehicle in populations with limited access to fortified foods.

5.5 Vitamin A

Vitamin A deficiency (VAD) remains endemic in large parts of Sub-Saharan Africa and South Asia, contributing to approximately 250,000-500,000 cases of childhood blindness annually. Egg yolk retinol content is directly responsive to dietary supplementation: hens supplemented with retinyl acetate or high levels of β -carotene (which hens partially convert to retinol) produce eggs with substantially elevated retinol content, potentially contributing to the vitamin A status of young children in deficiency-prone populations who consume eggs regularly (Pinotti *et al.*, 2022) [31]. Bioavailability of egg yolk retinol is high, benefitting from the lipid matrix that facilitates micellization during digestion.

6. Carotenoid and Pigment Enrichment

6.1 Lutein and Zeaxanthin

Lutein and zeaxanthin are dihydroxy xanthophyll carotenoids that accumulate selectively in the macula lutea of the human retina, where they function as high-efficiency

optical bandpass filters (attenuating short-wavelength blue light before it reaches the photoreceptors) and as localized antioxidants against photo-oxidative stress generated by light absorption in the outer segment membranes (Nolan *et al.*, 2023) ^[29]. Epidemiological data consistently demonstrate an inverse association between macular pigment optical density (MPOD) a surrogate measure of tissue lutein and zeaxanthin status and risk of age-related macular degeneration (AMD), the leading cause of irreversible vision loss in adults over 60 in high-income countries. The Age-Related Eye Disease Study 2 (AREDS2) demonstrated that lutein/zeaxanthin supplementation reduced the progression to advanced AMD by 10% relative to placebo in participants with intermediate AMD (Nolan *et al.*, 2023) ^[29].

Conventional egg yolk contains approximately 250-300 µg of lutein plus zeaxanthin per egg a modest absolute quantity but one characterized by exceptionally high bioavailability. The lipid-rich yolk matrix facilitates carotenoid incorporation into bile salt micelles during intestinal digestion, resulting in absorption efficiency approximately 2-3-fold greater than lutein from spinach or cooked kale at equivalent concentrations (Fernandez-García *et al.*, 2019) ^[12]. Designer eggs enriched with marigold petal extract (*Tagetes erecta*, the dominant commercial source of lutein esters), algal-derived zeaxanthin, or synthetic lutein preparations can achieve yolk lutein concentrations of 1,000-2,500 µg per egg, with transfer efficiencies from hen diet to yolk ranging from 10-25% depending on the chemical form and dietary inclusion rate (Cachaldora *et al.*, 2019) ^[4]. A 12-week, double-blind RCT demonstrated that daily consumption of two lutein-enriched eggs (providing approximately 1,200 µg lutein/egg) significantly increased MPOD as measured by heterochromatic flicker photometry and substantially elevated plasma lutein concentrations in adults with early-stage AMD compared with conventional egg consumption without significant changes in serum lipid profiles, addressing safety concerns about cholesterol (Nolan *et al.*, 2023) ^[29]. These findings position lutein-enriched eggs as a plausible dietary strategy for primary prevention and retardation of AMD progression.

6.2 Astaxanthin

Astaxanthin is a ketocarotenoid synthesized by the freshwater microalga *Haematococcus pluvialis* that exhibits antioxidant potency orders of magnitude greater than vitamin E in certain *in vitro* assay systems, attributed to its unique ketone and hydroxyl functional groups at both ionone ring ends, which allow electron donation on both sides of the polyene backbone (Kamath *et al.*, 2020) ^[19]. Hen supplementation with *H. pluvialis* meal or synthetic astaxanthin results in yolk deposition of this pigment, imparting a deep orange-red yolk color and potentially conferring anti-inflammatory, neuroprotective and exercise-recovery benefits to egg consumers. Human RCT data

specifically evaluating astaxanthin-enriched egg consumption as the intervention are currently limited most clinical astaxanthin research employs encapsulated supplements but the foundational mechanistic evidence and favorable safety profile warrant dedicated investigation (Kamath *et al.*, 2020) ^[19].

7. Protein Quality and Bioactive Peptide Considerations

Egg protein is among the highest quality animal proteins evaluated by any contemporary scoring system. By the DIAAS (Digestible Indispensable Amino Acid Score) framework the current FAO-endorsed gold standard cooked whole egg achieves a DIAAS of approximately 1.21 relative to the 0.5-year-old reference pattern, exceeding both bovine milk (DIAAS ~1.08) and beef (DIAAS ~1.10) and substantially outperforming plant proteins (FAO, 2023) ^[13]. The essential amino acids most frequently limiting in plant-based diets lysine, methionine and tryptophan are all present in the egg at favorable concentrations relative to human amino acid requirements, underpinning the nutritional complementarity of eggs in mixed diets.

While the gross amino acid composition of egg protein is relatively resistant to dietary manipulation of the laying hen it is genetically encoded in structural proteins research has increasingly explored the modification of hen diet to influence the bioactive peptide landscape generated during gastrointestinal proteolysis. Ovotransferrin-derived peptides (e.g., IRW, IQW) exhibit vasodilatory and antihypertensive activity through ACE-inhibitory mechanisms; lysozyme-derived fragments demonstrate antimicrobial activity against gram-positive pathogens; and ovomucin hydrolysates exhibit anti-influenza adhesion properties (Mine *et al.*, 2022) ^[26]. While these bioactive peptides emerge primarily post-digestion rather than being enriched through hen nutrition per se, they represent a compelling functional dimension of egg protein that extends well beyond simple nitrogen delivery. The impact of cooking method on protein digestibility warrants explicit consideration. In a controlled study, lightly cooked (poached or soft-boiled) eggs achieved protein digestibility of approximately 91%, compared with 51% for raw egg white the substantial gap explained by the anti-nutritional activity of raw avidin (which sequesters biotin) and raw ovomucoid (a trypsin inhibitor), both denatured by heat treatment (Evenepoel *et al.*, 2021) ^[10]. This finding carries practical relevance for designer egg consumption: the nutritional advantages of enrichment are fully realized only in appropriately cooked products.

8. Common myths and facts about designer eggs

Few foods in nutritional science carry as heavy a burden of misconception as the egg. The following section systematically addresses the most prevalent and consequential myths, contrasted with the current evidence base. Table 3 summarizes these comparisons in brief.

Table 3: Common myths about eggs and designer eggs compared with current evidence-based scientific consensus.

Common Myth	Evidence-Based Fact
Eggs raise LDL cholesterol and cause heart disease.	Dietary cholesterol raises LDL modestly and only in hyper-responders. In most healthy adults, egg consumption raises both LDL and HDL, preserving the ratio. Meta-analyses of 23 + trials found no significant association between up to 7 eggs/week and CVD incidence (Godos <i>et al.</i> , 2021; Fernandez & Calle, 2021) ^[14, 11] .
Designer eggs are nutritionally the same as regular eggs.	Compositional differences are measurable and clinically meaningful. Omega-3 eggs may contain 5-10× more DHA; selenium-enriched eggs can meet 60-100% of adult RDA per serving (Cherian, 2022; Surai & Fisinin, 2021) ^[6, 38] .
Free-range eggs are always superior to designer eggs.	Free-range eggs have modestly higher omega-3 and CLA, but differences are inconsistent. A caged hen supplemented with algal DHA will produce an egg with far more DHA than an unsupplemented free-range hen (Karsten <i>et al.</i> , 2019) ^[20] .
Eggs cause or worsen fatty liver disease.	Choline in egg yolk (~147 mg/egg) actively facilitates hepatic VLDL secretion, protecting against lipid accumulation. Prospective data do not support a causal link between moderate egg consumption and NAFLD (Zeisel, 2017) ^[47] .
Designer eggs are only relevant for high-income consumers.	Nutritionally vulnerable populations pregnant women, the elderly, vegetarians and those in micronutrient-deficient regions stand to benefit most. Eggs are a culturally embedded, relatively affordable vehicle for micronutrient delivery globally.

8.1 The Cholesterol Myth: Historical Origins and Current Evidence

The association between dietary cholesterol and cardiovascular disease risk was crystallized in the Seven Countries Study of the 1960s and institutionalized in the 1968 American Heart Association guidelines, which recommended limiting dietary cholesterol to 300 mg/day a value that a single conventional egg (containing approximately 212 mg) nearly exhausted. This recommendation was perpetuated for decades largely on the basis of the diet-heart hypothesis and observations in rabbits an obligate herbivore in which dietary cholesterol predictably induces atherosclerosis, unlike the human omnivore whose hepatic cholesterol synthesis is substantially down-regulated in response to dietary cholesterol intake.

Contemporary meta-analyses of prospective cohort studies have substantially revised this picture. A systematic review and meta-analysis of 23 randomized controlled trials found no significant effect of egg consumption on 10-year cardiovascular risk score and a large pooled analysis of 17 cohorts found no association between up to 1 egg per day and incident coronary heart disease or stroke in healthy individuals (Godos *et al.*, 2021) ^[14]. The 2020 Dietary Guidelines Advisory Committee removed the 300 mg/day cholesterol limit, reflecting the consensus that dietary cholesterol is not the primary driver of cardiovascular risk in the general population saturated fat and refined carbohydrate are more potent modulators of LDL particle size and number (Fernandez & Calle, 2021) ^[11]. The caveat that individuals with type 2 diabetes or familial hypercholesterolemia may exhibit heightened LDL sensitivity to dietary cholesterol warrants individualized guidance but this is a clinically defined exception, not a reason for population-wide egg restriction.

8.2 The Organic Equivalence Myth

A prevalent consumer belief holds that organic or free-range eggs are nutritionally equivalent to designer/enriched eggs, such that purchasing the former eliminates any justification for the latter. The reality is more nuanced. Free-range and organic eggs do exhibit modestly higher omega-3, CLA and carotenoid levels than conventional caged eggs, reflecting greater foraging on insects, grasses and plant material. However, these differences are inconsistent across studies varying substantially with season, stocking density, pasture quality and geographic location and are generally smaller in

magnitude than those achieved through targeted dietary supplementation (Karsten *et al.*, 2019) ^[20]. A hen consuming a flaxseed-or algae-supplemented diet in a caged environment will produce eggs with considerably more DHA than an unsupplemented free-range hen in winter with limited pasture access. "Organic" and "enriched" are distinct quality axes, not interchangeable claims.

9. Contraindications and Safety Considerations

Designer eggs represent a safe and beneficial dietary addition for the vast majority of consumers when consumed in reasonable quantities as part of a varied diet. The following considerations are relevant for specific clinical populations and at excessive consumption levels and are presented to support evidence-informed dietary guidance rather than to discourage the use of this valuable functional food category.

9.1 Egg Allergy

Egg allergy affects approximately 1.3-1.8% of children globally, representing the second most common pediatric food allergy after cow's milk and is mediated primarily by IgE antibodies targeting yolk phosvitin, livetin and albumen proteins ovalbumin, ovomucoid and ovotransferrin (Mine *et al.*, 2022) ^[26]. Designer eggs do not structurally modify egg proteins; dietary manipulation of the laying hen alters lipid and micronutrient composition without altering the fundamental allergenicity of egg proteins. However, novel feed additives introduced to achieve designer egg profiles specific algal species, leguminous seed meals, or novel protein concentrates should be systematically evaluated for potential indirect allergen transfer before commercial deployment, a gap that current regulatory frameworks for designer eggs do not uniformly address.

9.2 Omega-3 Overconsumption and Anticoagulation

Long-chain omega-3 fatty acids at very high doses (generally above 3 g/day of combined EPA + DHA) may prolong bleeding time through reduced thromboxane A₂-mediated platelet aggregation. This risk is theoretical rather than consistently demonstrated in clinical trials at dietary doses achievable through food consumption and the European Food Safety Authority (EFSA, 2023) ^[9] considers supplemental EPA + DHA intake of up to 5 g/day safe for adults without specific bleeding risk factors. Designer eggs, even if consumed at two per day, typically deliver 300-900 mg combined EPA + DHA well within safe ranges for the

general population. Patients receiving anticoagulant therapy (warfarin, novel oral anticoagulants) who simultaneously consume high-dose fish oil supplements and multiple omega-3-enriched eggs daily should monitor total omega-3 intake and consult their prescribing physician, though food-dose interactions remain clinically minor (Calder, 2020)^[5].

9.3 Selenium Toxicity

Selenium has the narrowest therapeutic-to-toxic window of any essential trace element. The adult UL for selenium is 400 µg/day and chronic intakes above this level are associated with selenosis manifesting as characteristic garlic-like breath odor (due to dimethylselenide exhalation), brittle hair and nails, peripheral neuropathy and in severe cases, hepatic necrosis (Surai & Fisinin, 2021; EFSA, 2023)^[38, 9]. A single selenium-enriched egg providing 40-80 µg selenium is safe within the context of a varied diet and represents no risk to general consumers, contributing 10-20% of the UL. Consumers who simultaneously use high-dose selenium supplements (often sold at 200 µg/tablet for antioxidant purposes) should be aware that combining supplemental selenium with regular enriched egg consumption could approach the UL, particularly in regions where natural soil selenium and therefore food selenium is already moderate. Clinical monitoring is warranted in such cases.

9.4 Vitamin D Hypervitaminosis

Vitamin D is a fat-soluble prohormone that accumulates in adipose tissue and the liver, making toxicity possible with excessive long-term intake in the absence of adequately controlled sun exposure data. Vitamin D hypervitaminosis defined by serum 25(OH)D concentrations exceeding 150 nmol/L is associated with hypercalcemia and its sequelae: nausea, vomiting, polyuria, nephrocalcinosis and soft tissue calcification (Holick *et al.*, 2022)^[18]. Designer eggs enriched to provide 15-25 µg vitamin D3 per egg are within or near EU Novel Food authorization parameters and daily consumption of one to two such eggs is unlikely to cause vitamin D toxicity in the general adult population whose baseline dietary D3 intake is low. Individuals already receiving prescribed pharmacological vitamin D supplementation should account for egg-derived vitamin D in their total intake assessment.

9.5 Iodine Sensitivity in Thyroid Disorders

The thyroid gland requires iodine for thyroid hormone synthesis, but individuals with autoimmune thyroid disorders Hashimoto's thyroiditis and Graves' disease may exhibit paradoxical responses to sudden increases in iodine intake. The Wolff-Chaikoff effect (temporary suppression of thyroid hormone synthesis in response to acute iodine load) and iodine-induced hyperthyroidism in autonomous thyroid nodules are recognized clinical phenomena (Haldemann *et al.*, 2022)^[17]. High-iodine designer eggs (providing >100 µg iodine/egg) are a relevant consideration for individuals with known thyroid autoimmunity or iodine-induced thyroid dysfunction and clinical guidance in this subgroup should be individualized. For the general population, iodine-enriched eggs represent a safe and beneficial public health intervention.

10. Bioavailability and Food Matrix Interactions

The nutritional value of designer eggs is not fully characterized by compositional analysis alone. The bioavailability of enriched nutrients the fraction absorbed, transported to target tissues and metabolized to active forms is critically determined by the food matrix, cooking method and dietary co-consumption patterns. Carotenoids (lutein, zeaxanthin, lycopene, β-carotene) in the yolk lipid matrix are incorporated into mixed bile salt micelles during upper gastrointestinal transit, a process facilitated by the concurrent digestion of yolk phospholipids and triglycerides. This micellarization efficiency accounts for the 2-3-fold bioavailability advantage of egg yolk carotenoids relative to vegetable-source carotenoids consumed with minimal fat (Fernandez-García *et al.*, 2019)^[12]. Cooking (particularly frying and scrambling with added fat) does not significantly reduce yolk carotenoid content and may modestly enhance absorption by improving lipid co-digestion. This makes the common dietary practice of combining eggs with other fat-containing foods nutritionally synergistic for carotenoid uptake.

A particularly important and underappreciated bioavailability advantage concerns the molecular form of omega-3 fatty acids in designer egg yolk. Unlike most fish oil supplements in which DHA and EPA are esterified to triglycerides or synthetic ethyl esters egg yolk DHA is incorporated almost exclusively into phospholipids (predominantly phosphatidylcholine). Phospholipid-bound DHA exhibits superior intestinal absorption and more efficient tissue incorporation into plasma and erythrocyte membranes compared with triglyceride-esterified DHA in several experimental systems, because phospholipids do not require pancreatic lipase-mediated hydrolysis before micellar incorporation (Lemahieu *et al.*, 2019)^[22]. This structural advantage may confer a bioavailability benefit to designer egg DHA relative to equivalent supplement doses that is not captured by simple compositional equivalence comparisons.

Selenium bioavailability from selenomethionine-enriched eggs approaches 90%, benefitting from the active transport mechanisms serving methionine absorption. This far exceeds the bioavailability of inorganic selenium forms and is comparable to or superior to many commercial selenium supplement forms (Surai & Fisinin, 2021)^[38]. Vitamin D and E bioavailability from the yolk matrix are similarly favored by the lipid-rich environment, with absorption efficiency enhanced by co-consumption of the whole egg (yolk + albumen) rather than egg white alone.

11. Consumer Acceptance, Sensory Quality and Market Dynamics

The commercial viability of designer eggs rests not only on their nutritional superiority but on whether consumers will purchase, prepare and regularly consume them. Sensory quality is the most frequent point of commercial failure in functional food development and omega-3-enriched eggs are particularly susceptible to this challenge. The primary sensory defect a fishy or oxidized off-flavor arises from the peroxidation of DHA and EPA in the yolk, generating volatile secondary oxidation products (hexanal, malondialdehyde, 4-hydroxynonenal) detectable by consumers at concentrations well below their chemical detection thresholds. This risk is effectively mitigated by: (i) substituting fish oil with microalgal DHA sources, which inherently contain more antioxidant stabilizers; (ii) co-

supplementing hen diets with α -tocopherol (≥ 150 mg/kg diet) or plant polyphenol extracts; and (iii) ensuring cold chain integrity from farm to consumer (Van Hecke *et al.*, 2018) [44].

Consumer willingness-to-pay (WTP) studies across European and North American markets reveal that 60-75% of primary household food purchasers are willing to accept a price premium of 15-30% above conventional egg prices for eggs with clearly communicated, evidence-backed health benefits, particularly omega-3 enrichment and vitamin D fortification (Mintel, 2023) [27]. Key barriers to purchase intention include: skepticism about health claim validity, confusion between enriched and organic/free-range designations and limited understanding of why specific micronutrients matter. Clear, standardized, regulatory-approved labeling specifying the enriched nutrient, quantity per egg and percentage of the adult RDA contributed per serving is consistently identified as the most powerful driver of consumer trust and purchase confidence (Verbeke *et al.*, 2021) [45].

12. Future Directions

12.1 Gene Editing and Precision Metabolic Engineering

CRISPR-Cas9 and base-editing technologies offer a fundamentally different and potentially more efficient route to egg enrichment than dietary manipulation: modifying the metabolic genetics of the laying hen itself. Proof-of-concept studies in rodent models have demonstrated that upregulation of Δ -6 desaturase (encoded by the FADS2 gene) improves ALA-to-DHA bioconversion efficiency by over 3-fold, while knockout of fatty acid elongase 5 (ELOVL5) redirects carbon flux toward DHA rather than shorter-chain metabolites (Van Eenennaam & Young, 2022) [43]. Translating these approaches to commercial poultry genetics remains contingent on the resolution of regulatory frameworks for gene-edited livestock products, which differ substantially between jurisdictions the United States has adopted a relatively permissive case-by-case framework, while the European Union has only recently begun revising its genetically modified organism regulations to accommodate gene-edited animals (Van Eenennaam & Young, 2022) [43]. The commercial timeline for gene-edited laying hens producing constitutively enriched eggs is realistically 10-15 years from current regulatory trajectories.

12.2 Microbiome-Mediated Biofortification

The laying hen's gut microbiome substantially influences nutrient absorption, metabolic conversion of dietary precursors and ultimately the compositional output of the egg. Precision probiotic supplementation specifically targeting commensal species in the *Lactobacillus*, *Bifidobacterium* and *Butyrivibrio* genera has been shown to improve dietary selenium bioavailability, enhance short-chain fatty acid production and modulate hepatic fatty acid metabolism in laying hens, with downstream effects on yolk fatty acid profiles (Ding *et al.*, 2020) [8]. The emerging concept of microbiome-assisted biofortification in which the gut ecosystem is deliberately structured to maximize nutrient transfer efficiency from diet to egg represents a promising, low-cost complement to dietary enrichment strategies that warrants dedicated investigation in prospective hen production trials.

12.3 Precision Nutrition Integration

The convergence of nutrigenomics, wearable biomarker monitoring and personalized dietary recommendation platforms creates a conceptual framework within which specific designer egg products could be tailored to individual nutritional risk profiles. An older adult with documented vitamin D insufficiency (serum 25(OH)D < 30 nmol/L), intermediate AMD and low plasma DHA status could be matched with an egg specifically enriched in 25(OH)D3, lutein/zeaxanthin and algal DHA a precision functional food approach that is technologically feasible but requires integration of clinical diagnostic data with food system supply chains not yet achieved at scale (Koletzko *et al.*, 2019) [21]. The maturation of digital health platforms and direct-to-consumer nutrient testing may accelerate this trajectory within the coming decade.

12.4 Sustainability and Life Cycle Assessment

The environmental footprint of egg production is substantially lower than that of beef, lamb, or farmed Atlantic salmon across greenhouse gas emissions, land use and freshwater consumption metrics. Per unit of DHA delivered, algal-DHA-enriched eggs may offer a more environmentally favorable nutritional profile than farmed salmon which relies on considerable quantities of wild-caught fishmeal and fish oil in its feed while also avoiding the antibiotic use and escapement concerns associated with aquaculture (Rumpold & Schlüter, 2020) [33]. Lifecycle assessments directly comparing omega-3 delivery vehicles designer eggs, fish oil capsules, algal DHA supplements and fatty fish consumption across full nutritional equivalence units (i.e., per gram of bioavailable DHA delivered) are needed to fully characterize these sustainability trade-offs and inform policy decisions regarding promotion of designer eggs within sustainable dietary guidelines.

12.5 Albumen as an Enrichment Target

The dominant focus of designer egg research on the lipid-rich yolk as the primary enrichment site reflects the yolk's favorable lipid matrix for fat-soluble nutrient incorporation. The albumen, however, represents an underexplored vehicle for water-soluble bioactive delivery. The albumen proteins themselves particularly ovotransferrin and lysozyme have inherent bioactive properties, but the matrix could theoretically be enriched with folate, B12, specific amino acids, or antimicrobial peptide precursors through targeted hen nutrition or genetic modification of albumen protein gene expression. This frontier remains largely unexplored and represents an opportunity for novel designer egg product development.

13. Conclusion

Designer eggs represent one of the most scientifically grounded and practically accessible approaches to functional food development available to food scientists and public health nutritionists. Through targeted dietary manipulation of the laying hen, measurable and clinically relevant elevations in omega-3 fatty acids, selenium, iodine, vitamins D and E, lutein and zeaxanthin are consistently achievable addressing some of the most prevalent nutritional deficiencies in contemporary global dietary patterns. The clinical evidence supporting health benefits across cardiovascular, ocular, immune and skeletal endpoints is substantive and the safety profile at population-relevant intake levels is well characterized. Future advances in gene

editing, microbiome science and precision nutrition promise to further refine and personalize the application of this versatile functional food. Designer eggs will not replace the need for dietary diversity, but they offer a compelling, evidence-backed tool in the public health nutritionist's arsenal particularly where supplement compliance is low and where the egg is already a culturally embedded dietary staple.

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