

Review

Poultry Meat and Eggs as an Alternative Source of n-3 Long-Chain Polyunsaturated Fatty Acids for Human Nutrition

Alice Cartoni Mancinelli ^{1,*}, Simona Mattioli ¹, Cornelia Twining ², Alessandro Dal Bosco ¹, Ann M. Donoghue ³, Komala Arsi ³, Elisa Angelucci ¹, Diletta Chiattelli ¹ and Cesare Castellini ¹

- ¹ Department of Agricultural, Food and Environmental Science, University of Perugia, Borgo XX Giugno, 74, 06100 Perugia, Italy; simona.mattioli@unipg.it (S.M.); alessandro.dalbosco@unipg.it (A.D.B.); elisa.angelucci@unipg.it (E.A.); diletta.chiattelli@libero.it (D.C.); cesare.castellini@unipg.it (C.C.)
- ² Department of Fish Ecology and Evolution, Eawag: Swiss Federal Institute of Aquatic and Technical Sciences, Seestrasse 79, 6047 Kastanienbaum, Switzerland; cornelia.twining@gmail.com
- ³ Poultry Production and Product Safety Research Unit, ARS, USDA, Fayetteville, AR 72701, USA; annie.donoghue@usda.gov (A.M.D.); karsi@uark.edu (K.A.)
- * Correspondence: alice.cartonimancinelli@unipg.it

Abstract: The beneficial effects of n-3 long-chain polyunsaturated fatty acids (n-3 LC-PUFA) on human health are widely known. Humans are rather inefficient in synthesizing n-3 LC-PUFA; thus, these compounds should be supplemented in the diet. However, most Western human diets have unbalanced n-6/n-3 ratios resulting from eating habits and the fact that fish sources (rich in n-3 LC-PUFA) are not sufficient (worldwide deficit ~347,956 t/y) to meet the world requirements. In this context, it is necessary to find new and sustainable sources of n-3 LC-PUFA. Poultry products can provide humans n-3 LC-PUFA due to physiological characteristics and the wide consumption of meat and eggs. The present work aims to provide a general overview of the main strategies that should be adopted during rearing and postproduction to enrich and preserve n-3 LC-PUFA in poultry products. The strategies include dietary supplementation of α -Linolenic acid (ALA) or n-3 LC-PUFA, or enhancing n-3 LC-PUFA by improving the LA (Linoleic acid)/ALA ratio and antioxidant concentrations. Moreover, factors such as genotype, rearing system, transport, and cooking processes can impact the n-3 LC-PUFA in poultry products. The use of a multifactorial view in the entire production chain allows the relevant enrichment and preservation of n-3 LC-PUFA in poultry products.

Keywords: poultry genotype; long-chain polyunsaturated fatty acids; antioxidants



Citation: Cartoni Mancinelli, A.; Mattioli, S.; Twining, C.; Dal Bosco, A.; Donoghue, A.M.; Arsi, K.; Angelucci, E.; Chiattelli, D.; Castellini, C. Poultry Meat and Eggs as an Alternative Source of n-3 Long-Chain Polyunsaturated Fatty Acids for Human Nutrition. *Nutrients* **2022**, *14*, 1969. <https://doi.org/10.3390/nu14091969>

Academic Editor: Stephen Cornish

Received: 10 April 2022

Accepted: 4 May 2022

Published: 8 May 2022

Publisher's Note: MDPI stays neutral with regard to jurisdictional claims in published maps and institutional affiliations.



Copyright: © 2022 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (<https://creativecommons.org/licenses/by/4.0/>).

1. Introduction

The beneficial functions of long-chain polyunsaturated fatty acids of the n-3 series (n-3 LC-PUFA) in human health are well-known, as well as the importance of having a lower n-6/n-3 fatty acids ratio in diets [1]. However, humans are rather inefficient in synthesizing LC-PUFA; consequently, a certain amount of these compounds need to be acquired directly from the diet [2]. The current eating patterns, mainly in Western countries, result in an excessive intake of n-6 with a consequent n-6/n-3 unbalanced ratio [3]. This has led to a need to increase the n-3 content of foods. However, the benefits of an increase in n-3 LC-PUFA consumption for human health are in contrast with the difficulty in finding sustainable sources of these fatty acids. Fish are one of the richest sources of n-3 LC-PUFA, but, due to the potential of low sustainability of both fishing and aquaculture, it is important to shift the focus to an n-3 source derived from terrestrial animals with higher nutritional value and possibly with lower environmental impacts.

It is well-known that, by altering the composition of animal feed, it is possible to modify the fatty acid profiles of products (e.g., milk, egg, meat [4]). It is important to stress that, due to the hydrogenated activity of microorganisms of the rumen in polygastric

animals, there are closer relationships between the fatty acid composition of feeds and animal products in monogastric species. For example, it has been reported [5] that rabbits fed a diet enriched with n-3 precursor (C18:3n-3, α -Linoleic acid, ALA) exhibited meat with higher levels of n-3 LC-PUFA. Progressive increases in the n-3 content of eggs have been shown in laying hens fed diets containing 10% and 20% of n-3 precursors [6].

This review aims to provide a general overview of the importance of n-3 LC-PUFA in human diets and focuses on ways to increase their content in terrestrial animal products. Due to its physiological characteristics (monogastric species and short rearing cycle) and the widespread consumption of meat and eggs, poultry is considered to provide suitable terrestrial sources of n-3 LC-PUFA. The various factors related to increasing and preserving n-3 LC-PUFA in chicken products throughout the production chain are also outlined. In particular, the effects of the nutritional strategies, genotype, and the adopted rearing system are discussed. Further, to preserve the obtained n-3 LC-PUFA, the transport of the birds to the slaughterhouse and the cooking processes are also addressed.

2. Evolution of Human Diet

Early records of human diet date back to the Paleolithic period when the development of small utensils made plant resources, such as roots and tubers, more accessible for human consumption [7]. A key event that influenced the evolution of several current human diets was the domestication of animals and the cultivation of plants. Furthermore, the development of technological processes changed the nutrient components related to “wild” foods. Compared with their domesticated relatives, wild animals have consistently low fat content [8]. Most fat in domesticated animals is characterized by high levels of saturated fatty acids (SFA), some of which can negatively impact human health in terms of cardiovascular disease risk (CVD [9,10]), while polyunsaturated fatty acid (PUFA) and mainly n-3 LC-PUFA show numerous positive effects [11], such as preventing pathological disorders (see Section 3.1). For example, the current human diets in the US contain 12% of the total energy as saturated fats [12], while this value in the Paleolithic diet was only 7.5% [13,14].

However, the main difference between current versus Paleolithic diets is not in terms of the total fat intake (Paleolithic diet about 35% of total energy intake versus current recommendation of 20–35%) but mainly the ratio between different PUFA [12]. During the early evolutionary history of the genus *Homo*, there was a strict balance between n-6 and n-3 PUFA. In particular, a significant amount of n-3 fatty acids was present in the foods commonly utilized by prehistoric humans, including meat from hunting animals, wild plants, eggs, and fish. The n-3 LC-PUFA are the major structurally significant and biochemically active components of the brain in all mammalian species [15]. The phenomenon described as “encephalization” proposes that the increase in the brain size in primates and humans is probably due to the availability of n-3 LC-PUFA in the diet during early human evolution [16]. However, dietary changes in the last 100 to 150 years have influenced the type and the amount of PUFA, as well as other bioactive molecules (e.g., antioxidant, essential amino acids, micronutrients, etc.) in the food.

The best available estimate of ancestral human intake showed a different ratio between n-6 and n-3 (about 2:1) [14,17]. In contrast, the estimated PUFA consumption for humans today in the USA is about 15 g/d, but the intake of n-6 LC-PUFA is 10-fold higher than n-3 LC-PUFA [18]. In EU countries, there is a wide variation in LC-PUFA intake [19], with the amount of Eicosapentaenoic (C20:5n-3, EPA) plus Docosahexaenoic (C22:6n-3, DHA) acid varying between 106 and 419 mg/d, which is below the daily recommendations (500 mg/d). In critical population groups (e.g., infants, children, adolescents, elderly, and pregnant/lactating women) the ALA intake is within the daily dose recommendation in 77% of the EU countries, whereas the n-3 LC-PUFA intake met the recommendations only in 26% of the European countries. These results indicate that the intake of n-3 and n-6 PUFA is suboptimal in specific population groups in Europe [20] and that their ratio is about 12 times higher than the recommendations [21] and has increased since 1961. Thus,

in Western countries, human diets are unbalanced in terms of PUFA, with a significant increase in n-6 and a decrease in n-3 LC-PUFA. Overall, during the last 100 years, the ratio between n-6 and n-3 has significantly increased to 20:1, whereas the recommendations suggest that this ratio should be less than 4:1 (Figure 1).

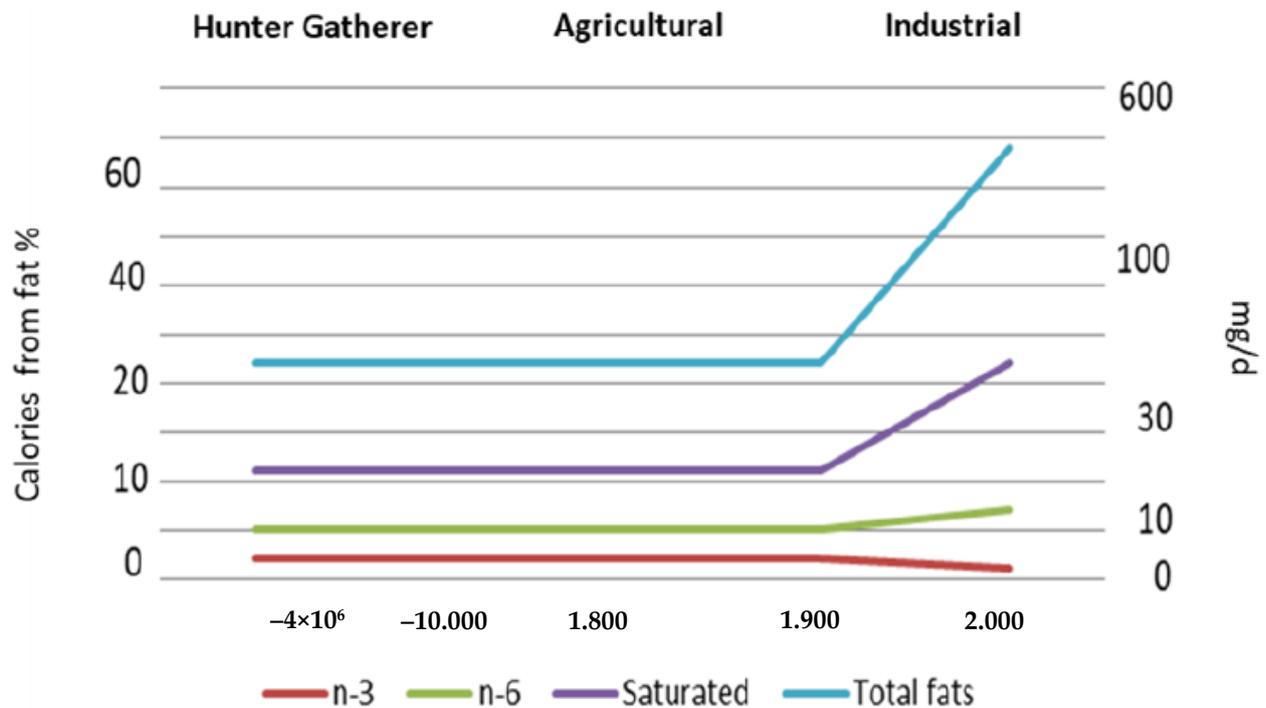


Figure 1. Estimated intake (mg/d) of n-3, n-6, saturated fatty acids, and total fats in relation to calories (%) provided by fat during human evolution. Data from Simopoulos, 2019 [22].

3. Notes on Metabolism of Essential Fatty Acids and Desaturase Activity (Details of Synthesis)

Linoleic acid (C18:2n-6, LA) and ALA are the precursors of n-6 and n-3 LC-PUFA, respectively. These precursors cannot be synthesized by mammals, including humans, and birds, and, for this reason, they are defined as essential fatty acids (EFA; [23]). The most physiologically important n-3 LC-PUFA are EPA and DHA, whereas Arachidonic acid (C20:4n-6, AA) is the most important n-6 LC-PUFA [23]. Both LA and ALA can be converted into long-chain metabolites through an elongation and desaturation metabolic process (Figure 2), which predominantly occurs in the liver. Other tissues (e.g., brain, testicles, epididymis, ovaries, muscles), although capable of synthesizing a certain amount of LC-PUFA, have lower metabolic efficiency [24–26]. The Δ 5- and Δ 6-desaturases enzymatic complex, controlled by the fatty acid desaturase 1 and 2 (FADS1 and FADS2) genes, introduces double bonds into the respective fatty acids (i.e., LA or ALA). The FADS2 acts twice, first at the C18 level and second after the conversion of the latter into C24 derivatives; accordingly, it is considered one of the main factors limiting LC-PUFA biosynthesis.

The conversion of ALA into EPA is in competition with the conversion of LA into AA because the biosynthesis of both n-3 and n-6 LC-PUFA requires the same enzymes [23] (Figure 2). This competition for desaturases and elongases in n-3 and n-6 LC-PUFA synthesis affects their relative concentration in tissues. Thus, animals fed diets rich in n-6 produce more LA metabolites, such as AA, compared to ALA metabolites, such as EPA and DHA, whereas higher ALA intake results in increased synthesis of n-3 LC-PUFA [26].

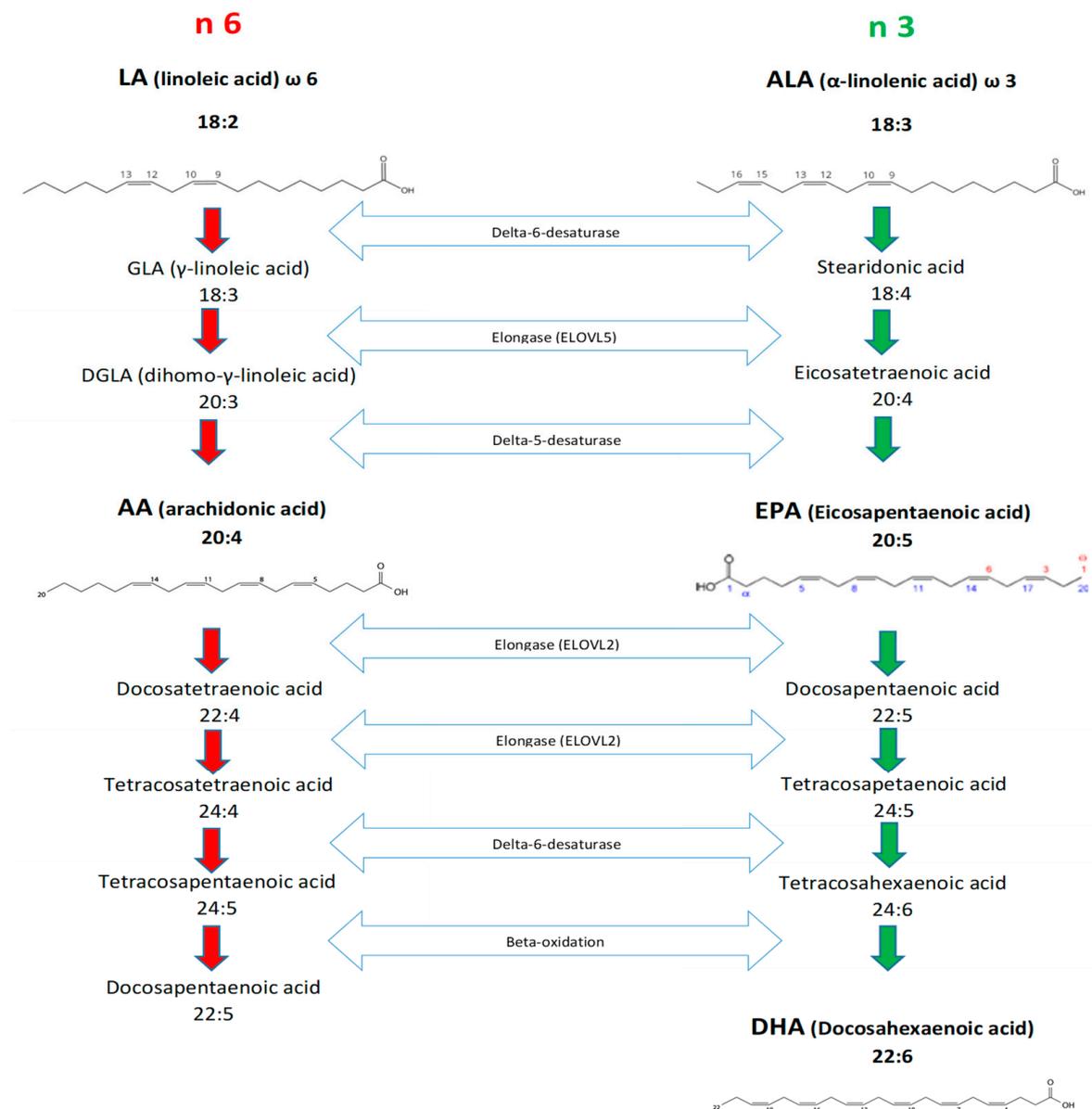


Figure 2. Metabolic pathways of n-6 and n-3 PUFA. The red arrows indicate the synthesis of n-6 and the green arrows the synthesis of n-3. The double blue arrows represent the enzymatic pathway.

These two PUFA families, ALA and EPA for the n-3 and AA for the n-6 series, are the precursors of the main compounds involved in the inflammatory response, such as prostaglandins (PGs), thromboxanes (TH), and leukotrienes (LT) [27]. Such molecules, called eicosanoids, have opposite functions: anti-inflammatory and anti-aggregating properties when synthesized by n-3 LC-PUFA, whereas pro-inflammatory and aggregating properties when derived by n-6 LC-PUFA. In particular, Cyclooxygenase (COX) is the key enzyme in the synthesis of PGs from AA, and it is present in two isoforms:

1. COX-1, a constitutive enzyme widely expressed in most tissues because it controls the synthesis of PGs involved in the regulation of homeostatic function;
2. COX-2, a specific enzyme, exerts its functions only during inflammatory processes; thus, PGs formed by COX-2 are principally involved as mediators of pain and inflammation [27,28].

The biosynthesis of PGs is triggered following the onset of extracellular stimuli. These stimuli, in turn, trigger the activity of phospholipase A2 (PLA2) and phospholipase C (PLC),

which cleaves phospholipids from the plasma membrane and increases the availability of fatty acids for the PGs synthesis by the COX enzyme (Figure 3). The ALA and EPA can be processed by COX-1 to generate PGs of the 3-series (PG₃, less inflammatory), while AA can be processed by COX-2 to generate prostaglandins of the 2-series (PG₂) or by epoxygenase and lipoxygenase to form epoxyeicosatrienoic acids (EETs), thromboxanes, leukotrienes, and hydroxyeicosatetraenoic acids (di-HETEsM) [29]. As previously reported, the PG₂ are highly inflammatory and responsible for the pathophysiological process of fever (e.g., prostaglandin E₂, PGE₂). The availability of ALA, EPA, or AA for the PGs synthesis is impacted by the composition of the membrane phospholipids, which, in turn, is influenced by the levels of n-6 and n-3 precursors in the diet.

A significant body of literature demonstrates that increased ingestion of n-3 PUFA is associated with a decreased PG₂ synthesis [3,30]. This is due to the replacement of AA with n-3 PUFA in the phospholipids, which, when released, attenuates the rate of PG₂ formation (AA-derived). Accordingly, modification of n-3 and n-6 PUFA (especially AA) availability with different strategies (diet, drugs, etc.) strongly affects the immune and inflammatory responses of the body [31]. Thus, the fatty acid composition of tissues can influence their inflammatory responses. This process of inflammation represents a physiological defense mechanism protecting the body from infection and diseases; however, it must be well-regulated in order to maintain homeostasis (inflammation vs. anti-inflammatory). Because n-6 PUFA content is much greater than n-3 PUFA in typical Western diets, controlling dietary AA allows a down-regulation of PG₂ synthesis and, consequently, anomalous inflammatory responses [32].

In this context, it is important to mention a new class of compounds, recently discovered, called isoprostanoids (IsoPs). The IsoPs are a series of PGs-like compounds produced by the free-radical-catalyzed peroxidation of fatty acids, independent of the COX [33,34]. On the basis of the LC-PUFA involved, IsoPs can be divided into different classes: F₂-IsoPs derived from AA oxidation; F₁, F₃, and F₄-IsoPs from ALA, EPA, and DHA, respectively [35]. Because of their specific derivation, IsoPs are considered a very sensitive marker of lipid peroxidation. Recent studies [36–38] have established that these molecules, besides being robust markers of oxidative damage, also exhibit a wide range of biological activities. F₂-IsoPs exert a vasoconstriction function, especially at the renal level; the F₄-IsoPs, also called neuroprostane (4-F₄t-NeuroP), is mainly present in brain tissue and increases its concentration with the onset of neurodegenerative disease. F₁-IsoPs, because of its origin from ALA, is considered the main oxidation biomarker in plants, enhancing its level under stress conditions. Due to issues with the imbalance ratio of n-6/n-3 in modern diets, it was recommended to increase the amount of n-3 in the human diet, and, subsequently, there has been an increased interest in the research towards the IsoPs derived from EPA and DHA. In fact, since n-3 LC-PUFA exert beneficial functions for human health, it is possible to hypothesize that their derivative compounds can also be beneficial.

Many studies report that a high dietary level of n-3 PUFA leads to the formation of F₃-IsoPs and F₄-IsoPs from non-enzymatic oxidation of EPA and DHA, respectively [26]. In addition, their abundance is also affected by the PUFA composition of different organs; for example, the brain and spermatozoa are particularly rich in n-3 LC-PUFA and also in F₄-IsoPs [26]. However, despite the importance of the IsoPs at the physiological level, further investigations are needed to better understand the different role and metabolic pathways involving such compounds and their relation with the LC-PUFA precursor.

3.1. Relevance of n-3 LC-PUFA in Human Nutrition

In the last few decades, the LC-PUFA compounds have been largely investigated for their nutritional value and for the numerous biological actions and therapeutic functions in different organs. The n-3 LC-PUFA are particularly abundant in the brain, retina, and reproductive cells and play important roles in many metabolic pathways, preventing pathological disorders, such as cardiovascular disease, reproductive dysfunction, chronic inflammatory diseases, depression, and deficiencies in the immune system [39,40].

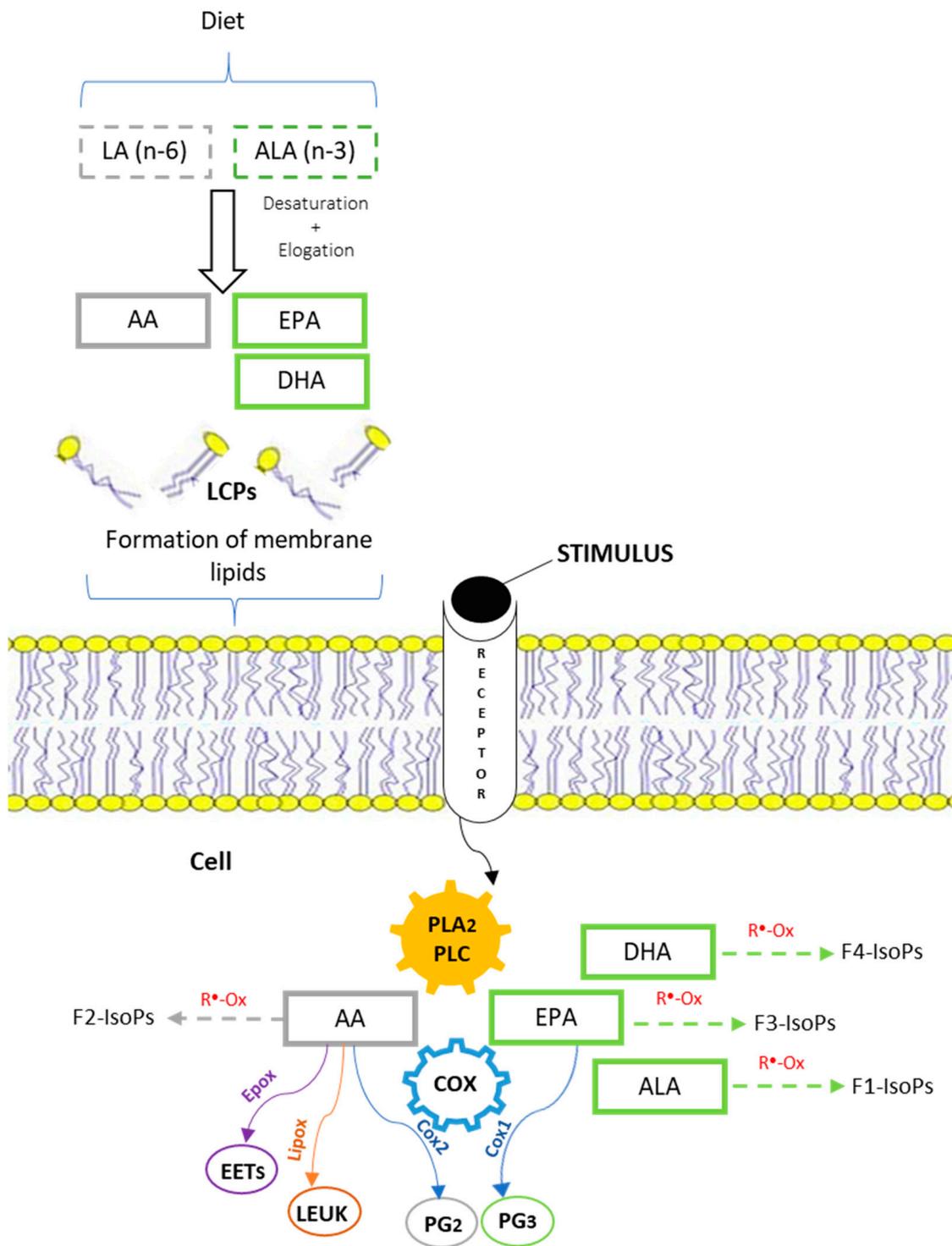


Figure 3. Schematic representation of PUFA metabolism, PGs, and IsoPs synthesis. The n-3 and n-6 precursors (ALA and LA) from the diet through desaturation and elongation processes form LC-PUFA: AA (n-6), EPA, and DHA (n-3). The LC-PUFA are incorporated into the phospholipids of plasma membrane. When external stimuli occur, the PLA₂ and PLC cleave phospholipids to increase the cell availability of AA, EPA, ALA, and DHA. The AA is processed by the COX₂ enzyme to form PG₂, or by epoxygenase and lipoxigenase to form epoxyeicosatrienoic acids (EETs) and leukotrienes (LEUK). The EPA is involved in the PG₃ synthesis by the COX₁ enzyme. Free radical peroxidation of LC-PUFA generates different classes of IsoPs. F₂-IsoPs derive from AA oxidation, while F₁, F₃, and F₄-IsoPs from ALA, EPA, and DHA, respectively.

As previously mentioned, humans are rather inefficient in synthesizing LC-PUFA [41] and, accordingly, they should be consumed directly through the diet. Thus, experts, such as the European Food Safety Authority (EFSA), have established n-3 nutritional recommendations in relation to age, sex, and body condition. It has been suggested that 250 mg/d is the minimum quantity of EPA and DHA required for an adult [42].

For pregnancy and lactation, considering the increased demand of n-3 LC-PUFA, the suggested intake is 350 to 450 mg/d of DHA, while, for young children (<24 months), the adequate intake is 100 mg/d of DHA. DHA is the main LC-PUFA recommended as it is a key component of the membrane lipids of the nervous system and adequate DHA concentration is linked to optimal brain development that occurs in the first 2 years of life [1]. In the fetus and newborn, the supply of DHA depends on the maternal diet since studies [43,44] showed that a high n-3 LC-PUFA intake by pregnant or lactating women can promote mental development in babies. On the contrary, low n-3 LC-PUFA concentration during the fetal period affects the brain volume, reducing its dimensions in childhood [45]. Moreover, in the brain, n-3 LC-PUFA, besides the formation of the plasma membrane, exert other functions, such as an increase in cognitive activity [46] and development of synaptic functionality and plasticity [47]. Indeed, a recognized beneficial effect of n-3 LC-PUFA consumption concerns neurodegenerative disorders, such as Parkinson's (PD) and Alzheimer's disease (AD) [48,49]. Accordingly, a lower concentration of DHA was found in the serum of patients affected by AD as compared to healthy people [50], suggesting that n-3 LC-PUFA could represent a preventative strategy against AD, especially when consumed in the early stage of the disease [51]. Numerous clinical trials were carried out to investigate the effects of n-3 consumption on the reduction in CVD; however, an open debate is underway regarding the efficacy. Recent studies support the hypothesis that the intake of n-3 LC-PUFA reduces the risk of CVD [52,53], but not all the research papers agree with this outcome [54] as varying experimental designs and the heterogeneity of the results render it difficult to find clear conclusions [55].

The EFSA [56] has performed numerous studies to determine the tolerable upper intake (UI) of n-3, concluding that a higher intake did not induce any adverse effect on human health; therefore, individuals could safely increase their daily n-3 LC-PUFA consumption.

The n-3 LC-PUFA represent about 30 to 50% of the membrane composition of sperm cells and are fundamental for reproductive activity by regulating the fluidity and the acrosomal responsiveness [57,58]. The high LC-PUFA concentration in the spermatozoa plasma membrane makes it vulnerable to lipid peroxidation [59]. Thus, the presence of oxidative stressors, such as obesity, sexually transmitted disease, alcohol, and tobacco use, could represent possible factors affecting male infertility [60,61].

The Western diet rich in saturated fat and n-6 PUFA induces obesity that is associated with many diseases, such as cancers, behavioral disorders, cardiovascular complications, and insulin resistance. Although these pathologies come from different causes and conditions, their onset is linked to the increase in n-6 PUFA and decrease in n-3 PUFA in the modern diet so that they are defined as diet-related chronic diseases. As previously reported, the overconsumption of n-6 PUFA increases the synthesis of PG_2 , with a pro-inflammatory effect. Moreover, it has been recently discovered that the AA-derived endocannabinoid compounds linking to their brain receptors are able to increase the appetite and food intake, worsening obesity status [62]. The AA is widely present in various cells and tissues so that it can be quickly converted into pro-inflammatory eicosanoids, increasing the chronic disorders [62]. The higher AA concentration with respect to EPA and DHA can lead to oxidative stress in the cell due to the increase in reactive oxygen species production [63]. Oxidative and inflammation status can negatively affect the reproductive function and elevate the risk of CVD, cancer, and other chronic diseases. Therefore, increasing the n-3 intake in humans in order to maintain a balanced n-6/n-3 ratio is essential for regulating body homeostasis.

3.2. Global Requirements for EPA and DHA

As previously reported, EFSA [42] provides the recommended minimum daily intake of EPA and DHA for different classes of population. Combining these data with those related to the world population classes [64,65], it is possible to estimate the annual global requirement for n-3 LC-PUFA (Table 1). As reported in Table 1, the annual global requirement for n-3 LC-PUFA (mainly EPA + DHA) to satisfy the need of the whole world population is about 722,960 t/y. The main source of n-3 is represented by fish; however, the supply of n-3 LC-PUFA from fish and fish products is insufficient to meet the world n-3 LC-PUFA demand [66]. Consequently, the estimated n-3 LC-PUFA deficit is about 347,956 t/y. It is noteworthy that such estimates do not take into account the most vulnerable groups of population (i.e., elderly and patients affected by physiological and metabolic disorders); thus, the amount of n-3 LC-PUFA deficit could be even higher. Within this context, it is not clear how to satisfy this enormous n-3 LC-PUFA deficit with the current foods. Accordingly, it is vital to develop alternative strategies for increasing n-3 PUFA and mainly n-3 LC-PUFA availability in common foods.

Table 1. Estimated global requirements of n-3 LC-PUFA and their availability from fish.

Population classes	n-3 LC-PUFA REQUIREMENT		
	n	EPA and DHA (mg/d)	EPA and DHA (t/y)
Total world population	7,922,857,397		
Adult individuals	7,903,361,753	250	356
Women in pregnancy and lactation	9747,822	400	1423
Young children (<24 months)	9,747,822	100	721,182
TOTAL			~722,960
AVAILABILITY			
Wild and farm-raised fish			100,000,000
50% of fish is suitable for human consumption			50,000,000
15% of the n-3 represent EPA and DHA			375,000
DEFICIT			~347,956

The table shows the estimation of the global annual deficit of n-3 LC-PUFA (t/y) calculated considering the n-3 LC-PUFA requirement in the main population classes and the amount of EPA and DHA provided by fish.

4. Sources of n-3 LC-PUFA and Strategies for Enriching Terrestrial Food

The importance of n-3 LC-PUFA in human health is evident, and they have been extensively described herein; however, the problem of how to increase the n-3 intake in the human diet is still unsolved. In this section, the principal n-3 LC-PUFA sources in the human diet (vegetable oil, fish, and terrestrial animal products) are described and new strategies to increase their availability in the food are discussed.

4.1. Vegetable Source

The beneficial effects of n-3 LC-PUFA on human health, and the low presence of these compounds in common foods, promoted the development of foods “enriched” in these fatty acids and the development of alternative terrestrial n-3 LC-PUFA sources.

The main sources of PUFA in human diets are vegetable oils. Many plants are able to synthesize ALA by successive desaturation of oleic acid and LA [67]. This process takes place in the plant leaves, roots, and seeds. Although vascular plants exhibit two distinct pathways for PUFA biosynthesis [68], fatty acid biosynthesis occurs almost exclusively in the plastids [69], and it is catalyzed by fatty acid synthase [70], which permits the synthesis of long-chain MUFA (monounsaturated fatty acids), such as erucic acid (C22:1), but the production of AA, EPA, and DHA is null or very scarce [71]. Most of the elongase enzymes involved in glycerolipid metabolism in plants have relatively broad substrate specificities capable of synthesis of fatty acids with 20 and 22 carbon atoms (C20 and C22 fatty acids [72]). Accordingly, LC-PUFA are only marginally synthesized because plants have a low desaturase activity on fatty acids with over 20 carbon atoms [72,73].

Some fungi, bryophytes (i.e., mosses and liverworts), and some marine and freshwater algae are capable of synthesizing LC-PUFA. However, the mechanisms of how these organisms are able to produce these compounds are not known [74–77]. In particular, these microorganisms, besides having the same desaturases present in the higher plants, show a higher affinity for the C20 and C22 fatty acids. Moreover, while some vascular plants are rich in fats, including ALA and other PUFA (e.g., flaxseed, canola), even when ALA constitutes a considerable fraction of fatty acids [78,79], the ALA content of most plants is low because they are low in fat [80–82].

4.2. Fish and Fish Products

Fish are the main source of n-3 LC-PUFA for humans, but the content in EPA and DHA varies by species and by how the fish are raised (i.e., wild or farm-raised, warm or cold water) [83]. For example, Pacific cod has higher EPA and DHA content compared to Atlantic cod (0.235 and 85 g/100g vs. 0.134 and 85 g/100g, respectively) [83].

Farm-raised and wild fish often contain similar amounts of EPA and DHA, but farmed fish are typically fed fish meal [84], which is not sustainable at a global scale because wild fish are used to produce fish meal [85]. In addition, the total SFA and PUFA content in farm-raised fish is higher compared to wild fish due to the higher n-6 concentrations in fish feeds [84]. Importantly, a number of marine fish of high commercial value for human consumption are unable to synthesize n-3 LC-PUFA. In fact, studies on hepatocytes from marine fish have shown very low ALA desaturation rates, without the production of EPA or DHA [86]. As previously mentioned, LC-PUFA synthesis depends on the desaturase and elongase activities. The relative inability of some marine fish to produce EPA and DHA can result from limited activities of either C18 or C20 elongases, as well as from low activity of $\Delta 5$ desaturase, which converts 20:4n-3 into EPA [87]. These enzymes appear to vary in their efficiency based upon the availability of PUFA in natural ecosystems [88,89]. Marine fish have large amounts of EPA and DHA in their diets, whereas freshwater fish consume diets that are more variable in n-3 LC-PUFA content. For example, carnivorous marine fish (e.g., tuna) lack functional desaturation and elongation enzymes, likely because they have little selective pressure to maintain synthesis in an environment where it is not strictly required [90]. Accordingly, many marine fish are only “accumulators” of n-3 LC-PUFA produced by lower trophic levels (i.e., marine phytoplankton). For example, phytoplankton rich in EPA and DHA include *Bacillariophyceae*, and *Chrysophyceae*; *Cryptophyceae*, *Prasinophyceae*, *Rhodophyceae*, *Xanthophyceae*, *Glaucophyceae* and *Eustigmatophyceae* (EPA sources), *Dinophyceae*, *Prymnesiophyceae*, and *Euglenophyceae* (DHA sources) [91,92]. These algae can also have high lipid contents, as well as high n-3 LC-PUFA concentrations (around 30–70% of DHA).

Although all fish originally evolved from marine lineages, in less n-3 LC-PUFA-rich freshwater environments, fish evolved an increased ability to synthesize n-3, including multiple species and populations with relatively recent marine origins [93].

Even though many studies have been carried out to increase the sustainability of aquaculture and, in particular, for the replacement of fish meal with other sources [94,95], fish are becoming progressively scarce and the over-exploitation of fishing areas worldwide is unsustainable. In addition, aquaculture cannot be considered a very sustainable source because, paradoxically, the feed used contains large quantities of wild fish [96]. Beyond the problems of sustainability, there is a growing concern with the methylmercury and polychlorinated biphenyls (PCB) levels in some species of fish, such as swordfish (*Xiphias gladius*), mackerel (including different species of pelagic fish, mostly from the family Scombridae family), and shark (*Selachimorpha*). Hites et al. [97] reported that levels of mercury and PCBs are higher in farm-raised salmon compared to wild salmon. The risks of methylmercury and PCB exposure are even more common in fish fed fish meal [98]. For this reason, the US Environmental Protection Agency [99], the US National Academy of Sciences [100], and additional international medical institutions recommend limiting the consumption of some species of fish.

Therefore, the choice of terrestrial animals as sources of n-3 LC-PUFA, and, thus, their ability to elongate and desaturate PUFA, must be carefully considered in order to find other sustainable, healthy, and safe products.

4.3. Terrestrial (Farmed) Animals

Terrestrial animals generally have lower content of n-3 LC-PUFA in their body than fish and a modest ability to synthesize LC-PUFA. Because the development of an embryo and fetus largely depends on LC-PUFA availability [101], females have higher n-3 LC-PUFA content and synthesis capacity than males [102]. Accordingly, female rats showed a higher DHA anabolism than males [102] and, thus, a higher liver concentration of DHA [103].

The most direct relation between the fatty acid profile of feed and that obtained in the food produced by it (meat, egg) is obtained in monogastric species. On the contrary, in ruminants, ingested fatty acids are hydrogenated by microorganisms of the rumen [104]. Stearic acid (C18:0) is the end product of this reaction, and it passes from the rumen into the abomasum, where it is digested and absorbed [105]. Fatty acids from the rumen are precursors of plasma synthesis of triglycerides that are mainly incorporated into the lipids of milk and adipose tissue [104]. Because of the hydrogenation activity of bacteria, the triglycerides of ruminant plasma, milk, and body fat result in a low PUFA content [106]. In ruminants, in order to bypass the rumen, PUFA must be protected for absorption in the duodenum [107]. In this way, the concentration of n-3 PUFA in milk can be increased fourfold by the inclusion of rumen-protected tuna oil in the diet of cows [108].

Unlike ruminants, in monogastric species (poultry, pig, rabbit), the PUFA profile of feed results in corresponding levels in their products; therefore, several strategies for enriching their content can be used. Thanks to these dietary strategies, there are a number of animal products in the market that are enriched in n-3 fatty acids, such as [109]:

1. Meat and poultry products (sausages, frankfurters, etc.);
2. Eggs and egg products (mayonnaise, etc.);
3. Milk and milk products (yoghurt, cheese, etc.).

It should be noted that the current meat and egg supply from monogastric animals is estimated to produce around 75.632 t/n-3 LC-PUFA/year (Table 2), which represents about 21 to 22% of the LC-PUFA annual world requirements, whereas other foods (beef, lamb meat) can add only a minor amount of n-3 LC-PUFA (<1%) [110,111]. It is likely that the major variation in lipid intake between populations reflects the true underlying differences in intakes and types of lipids consumed. Since it is difficult to change dietary habits, it is very important to modify the lipid profile of foods.

Table 2. Estimated global availability of n-3 LC-PUFA from terrestrial sources [110,111]).

	t/y	mg LC-PUFA/d	t LCP/y
Poultry	1.3×10^8	0.62	40,300
Eggs	7.7×10^7	0.35	26,845
Pork	9.4×10^7	0.18	8487
Total			75,632

The table shows the estimated annual availability of the n-3 LC-PUFA (mg/d or t/y) obtained from the monogastric livestock mostly consumed in the human diet.

In this context, poultry is particularly interesting for the following reasons:

- monogastric animal;
- short breeding cycle; meat-type chickens have an age at slaughtering of about 40 days;
- there are no religious limitations for poultry meat (or not as many as for pork or beef/lamb);
- lower environmental impact than other livestock productive chain [112] due to the high efficiency in converting feed into food;
- it is the most-consumed meat in the world;
- eggs easily meet the EFSA recommendation for n-3-enriched foods.

Poultry Meat and Eggs as Functional Foods

Poultry meat is rich in protein and is very suitable for human nutrition due to its low-fat content, high unsaturation degree of fatty acid, and low cholesterol levels [113]. It can even be considered to be a “functional food” as poultry meat can be beneficial for human health because it contains bioactive substances, such as vitamins and antioxidants, and has a balance of n-6 to n-3 ratio [114] close to the recommended ratio of 4:1.

It is also well-established that poultry eggs contain vitamins and minerals in addition to biologically active compounds with antimicrobial, immunomodulator, antioxidant, anti-cancer, or anti-hypertensive properties [115]. Owing to their high nutritional value and positive effects on human health, several of these compounds found in eggs are also selectively isolated and produced on an industrial scale [116]. Numerous studies have demonstrated that the quality of poultry meat and eggs can be further improved through various methods, including manipulating the diet to target certain functionalities, leading to the concept of the chicken as a bioreactor for the production of substances for humans [117–119].

5. n-3 LC-PUFA in Poultry Meat and Eggs, Strategies of Enrichment

Several studies have demonstrated that it is possible to increase the n-3 LC-PUFA content of animal origin products through different strategies, such as dietary supplementation, genetic selection, and rearing systems management. Moreover, pre- (transport to slaughterhouse) and post- (cooking) mortem factors can affect the preservation of the n-3 LC-PUFA enrichment in foods (see Sections 8 and 9).

5.1. Dietary Strategies for Broilers and Laying Hens

The n-3 LC-PUFA enrichment of livestock products is based on the dietary supplementation of n-3 PUFA precursors (ALA) from terrestrial sources or n-3 LC-PUFA from marine oils (Figure 4).

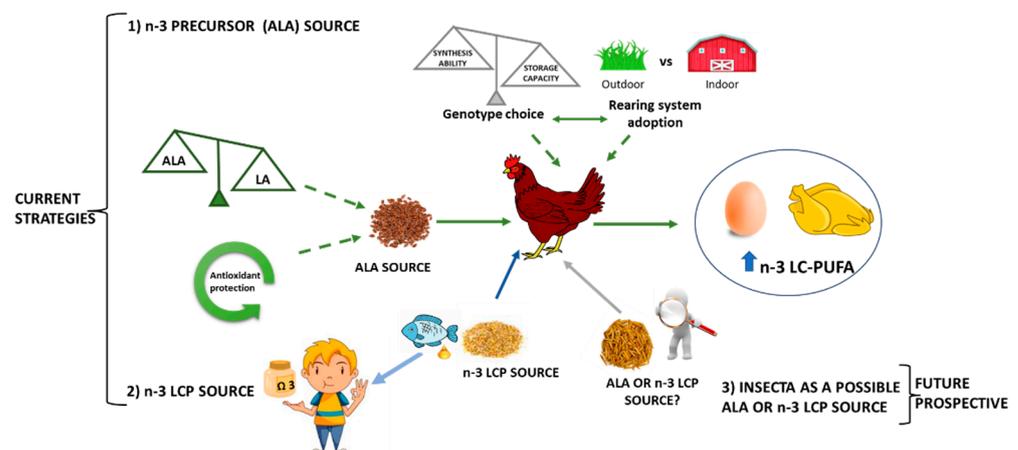


Figure 4. Graphical representation of the main dietary strategies to increase n-3 LC-PUFA in poultry products (egg and meat). The current dietary strategies consist of: (1) providing to animals n-3 precursor (ALA source) or (2) enriching animal feed with n-3 LC-PUFA. (3) A future perspective could be represented by insects as a source of n-3 precursors or n-3 LC-PUFA.

The first strategy implies that ALA must be converted by animal metabolism into LC-PUFA, while, in the second case, the LC-PUFA is simply absorbed, transferred, and stored in different tissues. Although this second strategy (e.g., addition of fish oil) easily enriches food in n-3 LC-PUFA, it is highly dependent upon wild fish production in marine ecosystems. In this view, it is important to consider that fish oil is an economically and environmentally expensive additive and the feed represents the major animal production cost [120]. Moreover, the fish oil approach also has other drawbacks [121,122], demonstrated

by the fact that its use in the chicken diet could negatively affect the sensory properties of the meat. Furthermore, it is important to point out that fish oil could be considered a constituent of the human diet [123]. In fact, the use of refined fish oil is much more metabolically efficient if administered directly to humans [124] without passing through the metabolism of livestock animals to produce food. Therefore, following these considerations, it is important to enforce the nutritional strategy based on the use of n-3 precursor. Further prospective could be represented by the introduction of insects to a poultry diet as a source of n-3 precursor or n-3 LC-PUFA. However, research still needs to be conducted to validate this aspect, and clarification in the regulations is needed to better understand how to manage the insects rearing (see Section 5.1.3).

By manipulating the broiler and the laying hen diets, it is possible to improve the conversion efficiency of ALA into n-3 LC-PUFA by exploiting the bird metabolism.

Despite broilers and laying hens exhibiting a different nutritional requirement, in order to efficiently administer ALA dietary supplementation, it is important to consider two main aspects (Figure 4):

1. The n-6/n-3 ratio of the diet. In fact, due the involvement of the same enzymes, the n-3 synthesis is in competition with the synthesis of the n-6 one; thus, the higher LA diet presence could reduce the production of EPA and DHA by favoring the AA synthesis [125];
2. The antioxidant supplementation (vitamin E, vitamin C, Selenium, etc.). Due to their double bonds, PUFA are very susceptible to oxidation, resulting in reduced shelf life of feed as well as meat and eggs. This can lead to a poor acceptance of the feed by the animals but also a poor acceptance of n-3 LC-PUFA-enriched products by the final consumers due to the development of unattractive colors or unpleasant tastes and aromas.

5.1.1. Dietary Enrichment for Broilers

In general, chicken meat represents a poor source of n-3 LC-PUFA; however, it is possible to increase their content by manipulating the broiler diet.

In this context, several studies [126,127] were conducted in order to evaluate the use of micro- and macroalgae in poultry nutrition as an n-3 LC-PUFA source. In particular, the use of Spirulina algae in the broiler diet increases the n-3 LC-PUFA content in meat, particularly EPA and DHA, with a positive effect also in the n6/n3 ratio [128]. The same results were obtained by Costa et al. [129] through the enrichment of the broiler diet with Brown macroalgae (e.g., *Laminaria digitata*). However, it is important to consider that both micro- and macroalgae are characterized by the presence of cell walls resistant to degradation by digestive enzymes. Thus, a high level of algae in an animal diet can compromise the nutrient digestibility, with a negative effect on the growth performance of animals [129].

Consequently, the main source of n-3 PUFA (ALA) used in the nutrition field is represented by flaxseed that is administered to the birds in different products, such as seeds, oil, or extract. Feeding turkeys with a diet containing 2.5% flaxseed oil from 16 days to 3 weeks of age before slaughter resulted in the recommended n-6/n-3 polyunsaturated fatty acids ratio of 4:1 in the meat [130].

Chickens, through the hepatic elongase and desaturase enzymes, are able to produce n-3 LC-PUFA from ALA [131]. Several studies demonstrated that it is possible to increase the level of n-3 LC-PUFA in chicken meat through the dietary supplementation of ALA. Other researchers did not obtain the same results, suggesting that there are other factors affecting the n-3 LC-PUFA biosynthesis. Diets with 8% of ALA increased the level of n-3 LC-PUFA in the chicken meat nine times as compared to the control group [132]. In contrast, Lopez-Ferrera et al. [133] reported that administering 8% of ALA in the diet obtained only a 3.6 times increase in n-3 LPC in the breast meat. The discrepancies found in the different studies are potentially the result of different durations of feeding ALA, the LA level in the diet, and genetic strain of birds in the studies (see Sections 7 and 8).

Furthermore, the ALA sources can affect the organoleptic properties of chicken meat; for example, 10% flaxseed addition in the last 14 days of the rearing cycle did not affect its taste or aroma [134], while 7% of flaxseed oil addition, in the same period, produced a fishy odor and taste in chicken meat [135].

As previously affirmed, when the level of PUFA increases, a higher antioxidant protection should be obtained. Vitamin E is the main antioxidant used for fatty acids supplementation and is generally added as α -tocopheryl acetate in poultry diets. Vitamin E supplementation in broiler diets not only increases the total tocopherols concentration in the different tissues (liver > adipose tissue > dark meat > white meat) but also enhances the antioxidant defense of major tissues, decreasing lipid peroxidation [136].

A body of literature also underlines that, in poultry, the effects of the dietary treatments are tissue-specific [132]. In other words, is not possible to establish a linear correlation among the ALA level provided with the diet and the concentration of n-3 LC-PUFA found in the different muscles (mainly breast and drumstick) in poultry meat.

Table 3 highlights some data from the literature. Although the studies were carried out in different experimental conditions, the same trend of n-3 LC-PUFA distribution in relation to the tissues was observed. In particular, when chickens are fed with ALA and EPA supplementation, a higher level of n-3 LC-PUFA was found in the liver compared to the breast [137] and drumstick [138]. Moreover, the drumstick data show a higher ALA content in respect to the breast; the latter exhibits a higher concentration of n-3 LC-PUFA (EPA and DHA) [139,140]. This is probably due to the different roles performed by the breast and drumstick muscle. It is well-known that the drumstick is involved in the movement and such activity consumes energy obtained through two main sources: carbohydrates and free fatty acids. The carbohydrates (mainly glycogen) are used for a fast and short contracting activity, whereas the free fatty acids are involved in the slow and prolonged exercise [141]. For this reason, the drumstick is rich in fats compared to the breast, and a portion is used (β -oxidation) for kinetic activity [142].

Table 3. n-3 fatty acid profile (mg/100 g of fresh tissue) in liver, breast, and drumstick tissues of broilers fed with different ALA and EPA sources.

Tissues	ALA+EPA g/kg of Diet	Time Feeding (d)	Genotype	ALA (C18:3)	EPA (C20:5)	DHA (C22:6)	TOTAL	References
Breast Drumstick	15	44	Ross 308	18.0 197	3 7	10 17	31 221	Cortinas, 2004 [139]
Breast Drumstick	25	21	Ross 308	147 258	13.5 10.8	31.5 17.5	192.0 286.3	Rymer, 2006 [140]
Liver Breast Drumstick	6.1	6	Cobb \times Ross 308	67.1 52.3 104.7	280.0 36.1 38.8	120.1 20.4 15.6	467.2 108.8 159.1	Shin, 2012 [138]
Breast Liver	10	30	Ross 308	185 407	56 275	86 335	327 1017	González-Ortiz, 2013 [137]

The table shows higher level of n-3 LC-PUFA in the liver compared to the other tissues. The drumstick exhibits a higher ALA content in respect to the breast.

In order to obtain meat rich in n-3 LC-PUFA, it is fundamental to consider both birds' ability to convert ALA into n-3 LC-PUFA and their storage efficiency of such compounds in the edible tissues [143].

5.1.2. Dietary Enrichment for Laying Hens

In poultry, as well as in other species [144,145], it has been demonstrated that the conversion of ALA is higher in females than in males [146]. As previously mentioned, sex has a significant effect on FADS expression and consequently on the n-3 LC-PUFA content of poultry products; adult female chickens have higher n-3 LC-PUFA synthesis ability due to needs of the chicken embryo. This is the reason why the efficiency of conversion of

ALA into LC-PUFA varies between chicken meat and eggs. Accordingly, egg yolk is a good source of n-3 LC-PUFA, especially DHA; indeed, standard egg yolks contain 0.1% EPA, 0.7% DHA, and 0.8% ALA [147]. Over the past 20 years, the influence of the dietary supplementation (mainly flaxseed) on the productive performance of the hens and the characteristics of the eggs have been extensively studied; however, the results reported are highly variable. Several authors reported a decrease in feed consumption [148,149], while others an increase [150] when flaxseed was added to the diet. Moreover, concerning the egg production, some authors showed an increase [151], while others reported a decrease [148] or no change of deposition rate [152]. Similar discordance was observed for egg weight [148,152]. These contradictory results can be ascribed to differences in experimental conditions; in fact, it is known that the age of hens and the genotype influence productive performance [153,154]. However, in these studies, the most important factor is represented by the diet formulation and, in particular, by mechanical/chemical treatments of raw materials. Flaxseed and other seeds used as ALA source often contain antinutritional factors (ANFs) that negatively affect the palatability and the digestion efficiency of the diet [118,155]. The cyanogenic glycosides present in the flaxseed are ANFs, responsible for impaired respiration rate in laying hens. Moreover, other ANFs, such as phytic acid and trypsin inhibitors, increased the intestinal viscosity [156] by reducing nutrient bioavailability [157]. These effects reduce hen performance and affect the egg quality [158]. However, by mechanical processing (extruding, heating, or by enzyme supplementation) of the raw seeds, it is possible to reduce/eliminate the ANFs [159,160]. Recent studies reported that the flaxseed extrusion [159], or the use of oils or soluble ingredients as ALA source, did not affect the productive performance in laying hens [118,161]. Therefore, in order to increase the n-3 LC-PUFA content in the eggs, it is important to use mechanically processed sources of ALA to avoid the effect of ANFs.

Regardless, laying diets rich in ALA, such as flaxseed, can increase the EPA and DHA content of their eggs [162,163]. Fraeye et al. [164] in their review concluded that dietary supplementation of flaxseed in laying hens proportionally increases the level of ALA in the yolk. Furthermore, amounts of DHA in yolk increase as well, but not in a linear way with respect to the level of flaxseed supplementation, suggesting that the LA/ALA ratio of the diet is one of the major factors affecting LC-PUFA synthesis. As previously mentioned, the common enzymatic pathway between n-3 and n-6 PUFA induces a competition for their synthesis; thus, the level of ALA and LA in the diet represents a crucial aspect. A recent meta-analysis [165] showed a linear relationship between the ALA levels in the diet and the amount of EPA, DHA, and total n-3 LC-PUFA in egg yolks, whereas a decrease in LA concentration was simultaneously observed. Authors reported that adding 100 g of ALA per kg in the diet resulted in 126 mg of DHA in the egg. Additionally, it was confirmed that, by increasing the LA content in the diet, and, consequently, the LA/ALA ratio, there was a linear decrease in the concentration of EPA and DHA in egg yolks. Given these relationships, diet composition (concentration of ALA, n-3 PUFA, and LA/ALA) can predict the content of EPA and DHA in the egg with a certain accuracy. However, it is important to consider that, even though numerous studies show that the decrease in LA and the increase of ALA in animal feed promotes the synthesis of DHA [166,167], other researchers reported that the continuous exposure to diets characterized by a high gap of LA to ALA decreased the egg weight [168]. Dong et al. [169] affirmed that hens fed fish oil supplementation over 16 weeks resulted in decreased egg weight. Thus, it is necessary to maintain a balanced LA/ALA ratio in the diet. Additionally, the age of hen is important and affects the n-3 LC-PUFA synthesis. Older hens characterized by higher liver dimensions are more efficient in metabolizing DHA from ALA compared to younger hens [164].

Flaxseed addition also affects other nutritional traits of egg. Mattioli et al. [117] show that the supplementation of the hen's diet with flax and alfalfa sprouts reduces plasma and egg cholesterol and increases the n-3 PUFA, vitamins (α -tocopherol, α - γ -tocotrienol, retinol), carotenes (β -carotene, lutein, zeaxanthin) and phytoestrogens (daidzein, equol, isolariciresinol).

It is important to underline that direct dietary alterations represent the main method for modifying LC-PUFA content in animal products; however, genetic [170] and rearing strategies [171] should not be ignored (see Sections 6 and 7).

5.1.3. Use of Insect and Earthworms as a Future Prospective

In recent years, many efforts have been made to find alternative and sustainable sources of feed for animals. One of the most promising sources is insects. Insects constitute more than 75% of the animal kingdom [172] and have potential as a sustainable source of food and feed. Most edible insects are rich in protein, lipids, and minerals. Insects and other invertebrates are natural protein sources for poultry and can potentially replace fish and soybean meal. Insects, due to their high reproductive potential, chemical characteristics, low water and space requirements, ability to use waste as feed, and low environmental impact, can be produced sustainably for livestock feed [173].

To increase sustainability, the diet for insects should consist of previously unused biomass, such as waste, low-value by-products, and non-traditional livestock feedstuffs.

However, currently, there are limitations on the types of feed allowed in insect rearing. Since insects are considered livestock, the ingredients allowed in insects' diets are subjected to EU regulations on feed hygiene, which restricts the use of food sources such as catering waste and processed animal protein [174]. In addition, the nutrient composition of insects varies with species, age, life stage, production, and processing conditions [175–177]. Even though significant variations exist in the nutrient composition of edible insects, many of these insects are high in monounsaturated and/or PUFA, mainly LA, ALA, and γ -linolenic acid [178], whereas LC-PUFA are scarce. The fatty acid composition of insects also depends on the environment where they develop [178]. Terrestrial species have lower LC-PUFA content, especially lower n-3 LC-PUFA, compared to species with an aquatic larval stage [179] due to the major differences in n-3 LC-PUFA availability in terrestrial plants versus aquatic primary producers such as algae.

Theoretically, insects could contribute to n-3 PUFA and LC-PUFA requirements for humans either by direct consumption of insects rich in n-3 PUFA or indirectly through consumption of fish and poultry products fed on such insects [180]. Among edible insects, black soldier flies (BSF, *Hermetia illucens*) are one of the most-studied, easily reared, and widely approved insects for use in poultry feeds in the US and Europe. BSF larvae can be raised on a wide range of substrates, resulting in insect biomass suitable for feeding animals [181]. The FA composition of insects such as BSF is partly determined by the composition of their diet, which can be modified to achieve a favorable n-6/n-3 ratio for animal feed. However, Hoc et al. [182], investigating the long-chain metabolic activity of BSF larvae, found that such insects produce scarcely any LC-PUFA. For example, even when fed high levels of ALA from flax-enriched diets, the larvae bioaccumulated around 13% of this fatty acid and metabolized approximately two-thirds of it into saturated fatty acid, such as lauric or myristic acid.

In a recent study, Rossi et al., [183] demonstrated an LC-PUFA enrichment in yellow mealworm (*Tenebrio molitor*) larvae only when they were reared on diets enriched in fish oil but not on sunflower or flaxseed oil diets. Such results suggest that these insects (i.e., *T. molitor* or BSF) are not able to convert ALA into n-3 LC-PUFA, and, thus, they are not a potential source of these compounds for consumption. According with the above-reported studies, both BSF and *Tenebrio molitor* showed a scarce efficiency to convert ALA into n-3 LC-PUFA. Therefore, they are mainly used as a source of protein [184,185] and lipids [186,187] as replacements of conventional ones.

However, studies on other insects, such as mealworms, have demonstrated that adding a source of n-3 fatty acids to their diet can significantly increase the n-3 PUFA content of some insect meals [183,188,189]. For instance, a recent study showed that an inclusion of 4% flax seed oil in diet resulted in 10- to 20-fold increase in n-3 fatty acid content in house crickets, lesser in mealworms and BSF [190]. Other studies also indicated an increase in the n-3 LC-PUFA content in BSF larvae when raised on oil seed

by-products, fish offals, or seaweed-based mediums [181,191,192]. Grass-fed poultry can naturally ingest various amounts of insects and earthworms. Earthworms are yet another alternative and little-explored source of protein and LC-PUFA for domestic animals. The use of earthworms presents a unique opportunity as earthworms can efficiently recycle the organic wastes and by-products from livestock operations into valuable feed sources for animals. Earthworms are high in essential amino acids and n-3 PUFA compared to other insects, and they can obtain EPA from their gut microflora instead of depending on dietary sources [193,194]. Earthworms are already part of a chicken's natural diet and their effect on inclusion in poultry diets has been reported occasionally from various geographical regions across Asia [195–200]. Dietary supplementation of earthworm meal (0.2–0.6%) improved performance in broilers as well as layers, especially in terms of laying performance, egg quality, and n-6/n-3 ratio of FA in egg yolks [198]. The content of n-3 FA, mainly EPA and DHA, is also important in the earthworm flour. For instance, the flour of *E. Andrei* is recommended as a source of protein and lipid in fish feed because of its high protein and PUFA content [201]. The current regulations in Western countries (EU and USA) do not allow the use of earthworms as an animal feed when reared on wastes. For example, the current EU legislation only permits certain insect species, including BSF, common house fly (*Musca domestica*), the Coleopteran species yellow mealworm, lesser mealworm (*Alphitobius diaperinus*), house cricket (*Acheta domesticus*), banded cricket (*Grylodes sigillatus*), and field cricket (*Gryllus spp.*), which have been reared on materials of vegetal origin in aquaculture feed, but prohibits raising insects or earthworms on catering or manure waste due to the risk of pathogen transmission [202]. However, there are fewer restrictions in Asia, Africa, and America in terms of insect species and rearing substrates.

More research is needed to identify the best substrates to raise earthworms, the safety of the feed sources, and the identification of the best species of earthworms to be reared for use in poultry and aquaculture.

6. Poultry Genotype

The current European regulations do not provide a clear classification of meat-type chicken genotypes, so most EU countries make this discrimination on the basis of daily weight gain (DWG). Therefore, broilers can be divided into three major groups based on their productivity:

1. Fast-growing genotypes (FG) are represented by birds used in intensive rearing systems reaching commercial weight in a very short time and characterized by a high breast yield (> 25% live weight). The most common genotypes are selected for precocity; at about 40 days of age their weight is more than 2.5 kg;
2. Medium-growing genotypes (MG), also known as slower-growing genotypes (SrG), are a recently recognized group and comprise some commercial chicken genotypes that are lower-performing than the FG ones, which is why the breed companies define them as SrG. These genotypes are less common in intensive rearing systems, but they are widely used in alternative rearing systems (e.g., free-range and organic);
3. Slow-growing genotypes (SG) are represented by breeds that are very important for maintaining biodiversity and genetic variability but, due to their low productive performance (growth rate and breast yield), are not utilized in intensive rearing systems. Thus, they are mainly used for niche-production in small-scale farms [203].

In the alternative systems, the presence of outdoor runs renders necessary the use of suitable genotypes with specific features, such as: kinetic and foraging activity, thermo-tolerance, and immune response of the organism [204,205]. It is widely known that FG genotypes use most of their dietary energy towards body growth, while the SG genotypes spend most of their energy on metabolic functions, such as thermoregulation, movement, and foraging [206]. Sirri et al. [207], comparing organically reared SG, MG, and FG chickens, found higher n-6 and n-3 PUFA concentration in the breast of SG, suggesting differential expression of genes encoding for desaturating enzymes. However, since SG and MG birds

are reported to eat more grass than FG genotypes [208], their higher dietary ALA intake could have also contributed to the higher degree of unsaturation in their meat.

Additional papers [209] confirmed that MG, and particularly SG chickens, showed a greater expression of FADS2 and FADS1 genes and a higher Δ^6 and Δ^5 activity and, consequently, higher n-3 LC-PUFA content in breast meat compared to FG genotypes. These findings agree with resource allocation theory [206] because the synthesis of n-3 LC-PUFA, due to additional cycles of elongation and desaturation (Figure 2 Section 3) and a final β -oxidation, is more metabolically expensive than that of the n-6. This could explain the preference of the FG, compared to SG, for n-6 [210]. As previously discussed, the competition between the two metabolic pathways (n-3 and n-6) affects the relative synthesis of different LC-PUFA. Dal Bosco et al. [211] show that the estimated Δ^5/Δ^6 -desaturase index was higher in the SG as compared to the FG genotypes and, consequently, the SG meat was characterized by a higher percentage of LC-PUFA (both n-3 and n-6) with respect to the FG meat. Accordingly, genetic selection for high performance unintentionally modified the expression of genes coding for enzymes involved in LC-PUFA synthesis as well as the relative enzymatic activity [212]. The relationship between genotype and desaturating ability has been demonstrated to have a significant impact on the PUFAs content of meat.

A recent paper [143] underlines that the presence of LC-PUFA in chicken meat depends on two main factors: the liver desaturase activity of the bird (conversion of ALA into LC-PUFA) and the storage capability of the LC-PUFA synthesized in tissues (mainly muscle). This study confirms the higher desaturase ability of the SG compared to the FG genotype but also points out the higher muscle storage of the FG chickens with respect to the SG as a consequence of their higher body fat content. SG birds more efficiently synthesize LC-PUFA, leading to a higher percentage of n-3 and n-6, but FG birds have a higher storage capability and, consequently, higher muscle fatty acids concentrations (in terms of mg fatty/100 g tissue). Overall, the research suggests that genetic effects on the desaturase and elongase activities are responsible for variation in n-3 LC-PUFA synthesis, making the genetic mechanisms behind the synthesis very interesting for future research. A new challenge in genetic selection should be to find a genotype with an optimum equilibrium between LC-PUFA synthesis and storage ability in order to increase the LC-PUFA content in chicken products. The identification of this genotype might represent an important goal not only for the agro-industry but also for the improvement of human nutrition.

For laying hens, genetic effects are less studied and probably less relevant because laying hens maintain high LC-PUFA conversion efficiency, mainly modulated by the reproductive efficiency (e.g., deposition rate) of their genetic strain [171].

7. Rearing System

The EU produces about 13.4 million tons of poultry meat [213], and 95% of this meat comes from intensive rearing systems [214]. These data show that poultry meat production from alternative systems (e.g., organic and free-range) is very limited. However, in recent years, there has been increasing demand for poultry meat and eggs grown utilizing these systems. In this context, France dominates the EU market by producing 16% of the total chicken meat with outdoor rearing systems [215].

In alternative poultry production, the presence of a pasture is crucial since the foraging birds spend a lot of time outdoors eating forage, pebbles, weeds, crop seeds, earthworms, and insects [204,216,217]. Many studies [171,217,218] have assessed the effects of pastures on poultry meat and egg quality. A natural pasture is rich in n-3 precursors, vitamins, and antioxidants that are transferred to chicken products, thus improving the fatty acid profile and the oxidative status of the meat and eggs with respect to those obtained from animals fed only commercial feedstuffs [216,219]. For example, the presence of a pasture reduced the n-6/n-3 ratio in SG chickens compared to the same strains when conventionally reared [220]. Dal Bosco et al. [216] also found a higher antioxidant intake in chickens reared outdoors compared to those reared indoors. Consequently, the antioxidant capacity of the

plasma and the antioxidant levels of the meat were also greater in the outdoor groups than in the indoor ones. Hens with access to a pasture produce eggs with at least twice as much vitamin A and E and n-3 LC-PUFA compared to hens with no access to a pasture [221]. The forage intake of hens also positively influences the FA profile of egg yolks. Organic-plus hens (local breed with 10 m²/hen of organic pasture) showed eggs with higher content of n-3 PUFA and lower concentrations of n-6 PUFA as compared to organic (commercial hens with 4 m²/hen of organic pasture) and conventional (commercial hens indoor-reared) eggs (Figure 5, [216]). Moreover, SG chickens reared outdoors are able to express all of their behavioral repertoire, mainly characterized by the foraging activity that naturally enriches their products with LC-PUFA and antioxidants [205].

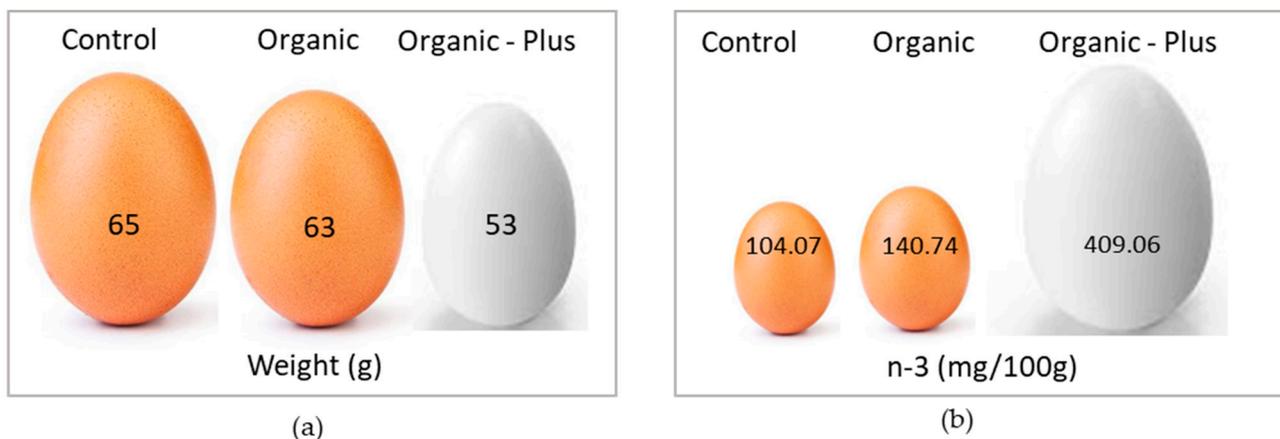


Figure 5. Comparison between (a) the weight (g) and (b) n-3 content (mg/100 g) of eggs from hens reared in conventional, organic, and organic-plus system. Conventional rearing system was characterized by commercial hens reared indoors; in the organic rearing system, commercial hens with 4 m²/hen of organic pasture were used, whereas organic-plus system consisted of local breed hens with 10 m²/hen of organic pasture. Data from Dal Bosco, 2016 [216].

When alternative rearing systems are adopted as a strategy to increase the LC-PUFA in animal products, it is important to choose suitable genotypes for this type of rearing (Section 6). It is widely recognized that FG genotypes, selected for high productive performance, being static animals, reared in outdoor conditions, exhibit low grazing behavior without exploiting the beneficial effects of a pasture [204,214].

8. Animals Transport

As discussed previously, the nutritional quality of poultry meat is affected by many factors, such as diet, genetic strain, rearing system, and animal welfare during the rearing phase. Other crucial factors that affect meat quality include the transport conditions of poultry from the farm to the slaughterhouse [222].

Chickens are captured and then, during transport, they are caged and deprived of water and feed and can be subjected to variable environmental conditions (i.e., noise, vibrations, and differences in temperature and humidity). European rules set several parameters for the humane transfer of poultry to the slaughterhouse; however, birds may still be subjected to high stress. Authors [223] show that chickens transported for 4h (which could be considered an average transport time in commercial conditions) exhibit higher stress (determined by a higher Heterophils/Lymphocytes ratio, an indicator of stress) compared to non-transported chickens. Research suggests that the effect of stress could be different in FG and SG strains [224]. Berri et al. [225] reported that SG suffer more during the lag phase between catching and slaughter due to their high kinetic activity (i.e., wing flapping) during transport and slaughtering. Accordingly, SG chickens, being more active, seem more sensitive to stress during transport compared to FG [226]. Moreover, the higher energy expenditure due to the metabolism increase caused by the stress consumes PUFA

via β -oxidation, reducing the concentration in body tissues [142]. Notably, the length of transport increases the proportion of saturated fatty acids of breast meat (mainly C16:0 and C18:0) and decreases PUFA (LA, AA, EPA, and DHA) content, likely due to greater formation of peroxides, as confirmed by higher TBARS values.

In addition, oxidative stress, caused by the length of transport, reduces the *in vivo* antioxidant content of the body and, consequently, enhances the post-mortem susceptibility of PUFA to lipid oxidation. Cartoni Mancinelli et al. [227], through the mobile poultry processing unit (MPPU), have proposed a possible solution applicable to small-scale farmers to avoid/reduce the transport of the birds. The MPPU, the first in Europe, consists of a truck equipped with a small slaughterhouse able to reach the poultry farm. At the moment, positive conclusions exist concerning the effect of MPPUs on animal welfare and meat quality.

Thus, to improve and preserve the nutritional quality of poultry meat, it is very important to pay particular attention both during the rearing period of animals (genotypes, breeding systems, diet, animal welfare, and health) and in the successive phases, such as slaughtering and cooking procedures.

9. Cooking Procedures

Meat is a perishable food; it has been reported that lipid oxidation of meat occurs in the following order: fish > poultry > pork > beef > lamb [228]. This different susceptibility to oxidation is attributed to the level of unsaturated fatty acids, as ALA oxidation is 20 to 30 times higher than LA [229], and to the antioxidant availability, in particular vitamin E stored in muscle cells. The cooking temperature of meat can result in the development of volatile organic compounds (VOC), which is largely attributed to the autoxidation of PUFA. The secondary products of lipid oxidation are responsible for warmed-over flavor production (WOF) [230]. The organoleptic rancidity due to the oxidative deterioration negatively affects acceptability for consumers. Pearson et al. [231] show that the temperature of 70 to 80 °C damages muscle membranes, which, in turn, induces the interaction of lipid oxidation catalysts with unsaturated fatty acids and consequent production of free radicals.

Among the free radicals, the thioradicals (e.g., oxidized proteins) are largely responsible for the WOF [232]. Poultry meat, due to its high content of LC-PUFA, is very sensitive to the oxidative process and, as previously reported, the genotype represents the main factor affecting the concentration of PUFA in meat. Indeed, it has been widely demonstrated that the SG chicken genotypes are more efficient at synthesizing n-3 LC-PUFA as compared to the FG strains. A recent study [233] compared the fatty acid, antioxidants, and VOC content of raw and cooked meat samples derived from four chicken genotypes with different growth rates. The study showed a 5.5 times increase in VOC production in cooked meat compared to raw meat across genotypes. However, the VOC production level was related to the LC-PUFA content in the raw meat and to the genotype. Consequently, the SG meat was considered “more vulnerable” due to the lower content of antioxidants as compared with the FG genotype [233]. In fact, the SG birds, due to their innate higher kinetic activity with respect to FG, consume the dietary antioxidants also to balance the oxidative process induced by movement [234]. In order to contain the losses of n-3 LC-PUFA, the meat antioxidants/LC-PUFA ratio should be considered as these could be altered by the cooking process.

10. Conclusions

The health importance of n-3 LC-PUFA in humans, together with the inefficiency of n-3 LC-PUFA synthesis, has increased interest in enriching foods in these compounds. Poultry can be considered a suitable animal model for studying n-3 LC-PUFA enrichment strategies in terms of rearing cycle practices and post-mortem processes. The main method of dietary manipulation consists of supplementation of n-3 PUFA precursors and vitamin E without compromising the diet LA/ALA balance. The genotype choices also have an important role in determining the poultry n-3 LC-PUFA content since it is necessary to consider both

the bird's ability to convert ALA into n-3 LC-PUFA and the deposition of such compounds into the edible tissues of chickens. When alternative rearing systems are used as a strategy to increase the n-3 LC-PUFA in animal products, due to the presence of ALA in grass and insects, it is crucial to adopt an explorative genotype able to use the available pasture. In order to preserve the n-3 LC-PUFA accumulated by the chickens during the rearing cycle in poultry products, it is also important to pay attention to the next steps, such as animal transport to the slaughterhouse and cooking procedures. For both processes, it is essential to reduce the duration and ensure an adequate quantity of dietary antioxidants in order to preserve the products' quality. For enriching and preserving the n-3 LC-PUFA in poultry products, a multifactorial approach should be adopted that encourages the use of multiple strategies throughout the entire production chain.

Further research efforts are still needed to clearly define the storage efficiency of the different strategies for the enrichment of poultry meat and eggs. Certainly, in the current world context, with insufficient n-3 LC-PUFA supplies for human nutrition, it is necessary to apply responsible and sustainable approaches, including:

1. avoiding livestock and human competition for n-3 LC-PUFA;
2. developing livestock systems with the best conditions for bio-conversion of n-3 precursors into n-3 LC-PUFA.

Author Contributions: Conceptualization, A.C.M. and C.C.; methodology, A.C.M. and C.C.; validation, S.M., C.T., A.D.B., A.M.D. and K.A.; investigation, A.C.M., C.C., S.M. and A.D.B.; resources, C.C.; data curation, A.C.M. and C.C.; writing—original draft preparation, A.C.M.; writing—review and editing, C.T., A.M.D. and K.A.; visualization, E.A. and D.C.; supervision, C.C. and A.M.D.; project administration, C.C.; funding acquisition, C.C., All authors have read and agreed to the published version of the manuscript.

Funding: This research was funded by PRIN2017, grant number 2017S229WC.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: Not applicable.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Van Dael, P. Role of N-3 Long-Chain Polyunsaturated Fatty Acids in Human Nutrition and Health: Review of Recent Studies and Recommendations. *Nutr. Res. Pract.* **2021**, *15*, 137. [[CrossRef](#)] [[PubMed](#)]
2. Goyens, P.L.; Spilker, M.E.; Zock, P.L.; Katan, M.B.; Mensink, R.P. Conversion of α -linolenic acid in humans is influenced by the absolute amounts of α -linolenic acid and linoleic acid in the diet and not by their ratio. *Am. J. Clin. Nutr.* **2006**, *84*, 44–53. [[CrossRef](#)] [[PubMed](#)]
3. Mariamenatu, A.H.; Abdu, E.M. Overconsumption of Omega-6 Polyunsaturated Fatty Acids (PUFAs) versus Deficiency of Omega-3 PUFAs in Modern-Day Diets: The Disturbing Factor for Their “Balanced Antagonistic Metabolic Functions” in the Human Body. *J. Lipids* **2021**, *2021*, 8848161. [[CrossRef](#)]
4. Mollica, M.; Trinchese, G.; Cimmino, F.; Penna, E.; Cavaliere, G.; Tudisco, R.; Musco, N.; Manca, C.; Catapano, A.; Monda, M.; et al. Milk Fatty Acid Profiles in Different Animal Species: Focus on the Potential Effect of Selected PUFAs on Metabolism and Brain Functions. *Nutrients* **2021**, *13*, 1111. [[CrossRef](#)] [[PubMed](#)]
5. Dal Bosco, A.; Castellini, C.; Bianchi, L.; Mugnai, C. Effect of Dietary α -Linolenic Acid and Vitamin E on the Fatty Acid Composition, Storage Stability and Sensory Traits of Rabbit Meat. *Meat Sci.* **2004**, *66*, 407–413. [[CrossRef](#)]
6. Ferrier, L.K.; Caston, L.J.; Leeson, S.; Squires, J.; Weaver, B.J.; Holub, B.J. Alpha-Linolenic Acid- and Docosahexaenoic Acid-Enriched Eggs from Hens Fed Flaxseed: Influence on Blood Lipids and Platelet Phospholipid Fatty Acids in Humans. *Am. J. Clin. Nutr.* **1995**, *62*, 81–86. [[CrossRef](#)]
7. Simopoulos, A.P. Evolutionary Aspects of Diet: The Omega-6/Omega-3 Ratio and the Brain. *Mol. Neurobiol.* **2011**, *44*, 203–215. [[CrossRef](#)]
8. Naughton, J.M.; O’Dea, K.; Sinclair, A.J. Animal Foods in Traditional Australian Aboriginal Diets: Polyunsaturated and Low in Fat. *Lipids* **1986**, *21*, 684–690. [[CrossRef](#)]
9. Jiang, J.; Xiong, Y.L. Natural antioxidants as food and feed additives to promote health benefits and quality of meat products: A review. *Meat Sci.* **2016**, *120*, 107–117. [[CrossRef](#)]

10. Salter, A.M. Dietary fatty acids and cardiovascular disease. *Animal* **2013**, *7*, 163–171. [[CrossRef](#)]
11. Calder, P.C. Marine Omega-3 Fatty Acids and Inflammatory Processes: Effects, Mechanisms and Clinical Relevance. *Biochim. Biophys. Acta Mol. Cell Biol. Lipids* **2015**, *1851*, 469–484. [[CrossRef](#)]
12. Lupton, J.R.; Brooks, J.; Butte, N.F.; Caballero, B.; Flatt, J.P.; Fried, S.K. *Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids*; National Academy Press: Washington, DC, USA, 2002; Volume 5, pp. 589–768.
13. Cordain, L.; Miller, J.B.; Eaton, S.B.; Mann, N.; Holt, S.H.A.; Speth, J.D. Plant-Animal Subsistence Ratios and Macronutrient Energy Estimations in Worldwide Hunter-Gatherer Diets. *Ann. J. Clin. Nutr.* **2000**, *71*, 682–692. [[CrossRef](#)] [[PubMed](#)]
14. Eaton, S.B.; Eaton, S.B.; Sinclair, A.J.; Cordain, L.; Mann, N.J. Dietary Intake of Long-Chain Polyunsaturated Fatty Acids during the Paleolithic. *World Rev. Nutr. Diet* **1998**, *83*, 12–23.
15. Sinclair, A.J. Incorporation of radioactive polyunsaturated fatty acids into liver and brain of developing rat. *Lipids* **1975**, *10*, 175–184. [[CrossRef](#)] [[PubMed](#)]
16. Crawford, M.A. The Role of Dietary Fatty Acids in Biology: Their Place in the Evolution of the Human Brain. *Nutr. Rev.* **1992**, *50*, 3–11. [[CrossRef](#)]
17. Cordain, L.; Eaton, S.; Miller, J.B.; Mann, N.; Hill, K. The paradoxical nature of hunter-gatherer diets: Meat-based, yet non-atherogenic. *Eur. J. Clin. Nutr.* **2002**, *56*, S42–S52. [[CrossRef](#)] [[PubMed](#)]
18. Raatz, S.K.; Conrad, Z.; Jahns, L. Trends in linoleic acid intake in the United States adult population: NHANES 1999–2014. *Prostaglandins Leukot. Essent. Fat. Acids* **2018**, *133*, 23–28. [[CrossRef](#)]
19. Harika, R.K.; Eilander, A.; Alssema, M.; Osendarp, S.J.; Zock, P. Intake of Fatty Acids in General Populations Worldwide Does Not Meet Dietary Recommendations to Prevent Coronary Heart Disease: A Systematic Review of Data from 40 Countries. *Ann. Nutr. Metab.* **2013**, *63*, 229–238. [[CrossRef](#)]
20. Sioen, I.; Van Lieshout, L.; Eilander, A.; Fleith, M.; Lohner, S.; Szommer, A.; Petisca, C.; Eussen, S.; Forsyth, S.; Calder, P.C.; et al. Systematic Review on N-3 and N-6 Polyunsaturated Fatty Acid Intake in European Countries in Light of the Current Recommendations—Focus on Specific Population Groups. *Ann. Nutr. Metab.* **2017**, *70*, 39–50. [[CrossRef](#)]
21. Schmidhuber, J.; Traill, W.B. The changing structure of diets in the European Union in relation to healthy eating guidelines. *Public Health Nutr.* **2006**, *9*, 584–595. [[CrossRef](#)]
22. Simopoulos, A.P. Genetic Variation and Evolutionary Aspects of Diet. In *Antioxidant Status, Diet, Nutrition, and Health*, 1st ed.; Papas, A., Ed.; CRC Press: Boca Raton, FL, USA, 2019; pp. 64–89.
23. Stark, A.H.; Crawford, M.A.; Reifen, R. Update on alpha-linolenic acid. *Nutr. Rev.* **2008**, *66*, 326–332. [[CrossRef](#)]
24. Castellini, C.; Mattioli, S.; Moretti, E.; Cotozzolo, E.; Perini, F.; Dal Bosco, A.; Signorini, C.; Noto, D.; Belmonte, G.; Lasagna, E.; et al. Expression of Genes and Localization of Enzymes Involved in Polyunsaturated Fatty Acid Synthesis in Rabbit Testis and Epididymis. *Sci. Rep.* **2022**, *12*, 2637. [[CrossRef](#)] [[PubMed](#)]
25. Mattioli, S.; Dal Bosco, A.; Maranesi, M.; Petrucci, L.; Rebolgar, P.G.; Castellini, C. Dietary Fish Oil and Flaxseed for Rabbit Does: Fatty Acids Distribution and $\Delta 6$ -Desaturase Enzyme Expression of Different Tissues. *Animal* **2019**, *13*, 1934–1942. [[CrossRef](#)] [[PubMed](#)]
26. Mattioli, S.; Collodel, G.; Signorini, C.; Cotozzolo, E.; Noto, D.; Cerretani, D.; Micheli, L.; Fiaschi, A.; Brecchia, G.; Menchetti, L.; et al. Tissue Antioxidant Status and Lipid Peroxidation Are Related to Dietary Intake of n-3 Polyunsaturated Acids: A Rabbit Model. *Antioxidants* **2021**, *10*, 681. [[CrossRef](#)] [[PubMed](#)]
27. Tapiero, H.; Ba, G.N.; Couvreur, P.; Tew, K. Polyunsaturated fatty acids (PUFA) and eicosanoids in human health and pathologies. *Biomed. Pharmacother.* **2002**, *56*, 215–222. [[CrossRef](#)]
28. Khan, A.A.; Iadarola, M.; Yang, H.-Y.T.; Dionne, R.A. Expression of COX-1 and COX-2 in a Clinical Model of Acute Inflammation. *J. Pain* **2007**, *8*, 349–354. [[CrossRef](#)]
29. Mattos, R.; Staples, C.R.; Thatcher, W.W. Effects of dietary fatty acids on reproduction in ruminants. *Rev. Reprod.* **2000**, *5*, 38–45. [[CrossRef](#)]
30. Carneiro, L.C.; Williams, E.J.; Saut, J.P.E.; dos Santos, R.M.; Celeghini, E.C.C. The Effect of N-3 Polyunsaturated Fatty Acid Supplementation on Immune and Reproductive Parameters in Dairy Cows: A Review. *Braz. J. Vet. Res. Anim. Sci.* **2021**, *58*, e175224. [[CrossRef](#)]
31. Kolobarić, N.; Drenjančević, I.; Matić, A.; Šušnjara, P.; Mihaljević, Z.; Mihalj, M. Dietary Intake of N-3 Pufa-Enriched Hen Eggs Changes Inflammatory Markers' Concentration and Treg/Th17 Cells Distribution in Blood of Young Healthy Adults—A Randomised Study. *Nutrients* **2021**, *13*, 1851. [[CrossRef](#)]
32. Calder, P.C. Omega-3 Fatty Acids and Inflammatory Processes: From Molecules to Man. *Biochem. Soc. Trans.* **2017**, *45*, 1105–1115. [[CrossRef](#)]
33. Morrow, J.D.; Hill, K.E.; Burk, R.F.; Nammour, T.M.; Badr, K.F.; Roberts, L.J. A Series of Prostaglandin F₂-like Compounds Are Produced in Vivo in Humans by a Non-Cyclooxygenase, Free Radical-Catalyzed Mechanism. *Proc. Natl. Acad. Sci. USA* **1990**, *87*, 9383–9387. [[CrossRef](#)]
34. Signorini, C.; Moretti, E.; Collodel, G. Role of isoprostanes in human male infertility. *Syst. Biol. Reprod. Med.* **2020**, *66*, 291–299. [[CrossRef](#)] [[PubMed](#)]
35. Milne, G.L.; Yin, H.; Morrow, J.D. Human Biochemistry of the Isoprostane Pathway. *J. Biol. Chem.* **2008**, *283*, 15533–15537. [[CrossRef](#)] [[PubMed](#)]

36. Galano, J.M.; Lee, Y.Y.; Oger, C.; Vigor, C.; Vercauteren, J.; Durand, T.; Giera, M.; Lee, J.C.Y. Isoprostanes, Neuroprostanes and Phytprostanes: An Overview of 25 Years of Research in Chemistry and Biology. *Prog. Lipid Res.* **2017**, *68*, 83–108. [[CrossRef](#)] [[PubMed](#)]
37. Molnár, P.J.; Der, B.; Borsodi, K.; Balla, H.; Borbás, Z.; Molnár, K.; Ruisanchez, É.; Kenessey, I.; Horváth, A.; Keszthelyi, A.; et al. Isoprostanes Evoke Contraction of the Murine and Human Detrusor Muscle via Activation of the Thromboxane Prostanoid TP Receptor and Rho Kinase. *Am. J. Physiol. Ren. Physiol.* **2021**, *320*, F537–F547. [[CrossRef](#)]
38. Wu, J.; Fang, S.; Lu, K.T.; Wackman, K.; Schwartzman, M.L.; Dikalov, S.I.; Grobe, J.L.; Sigmund, C.D. EP3 (E-Prostanoid 3) Receptor Mediates Impaired Vasodilation in a Mouse Model of Salt-Sensitive Hypertension. *Hypertension* **2021**, *77*, 1399–1411. [[CrossRef](#)] [[PubMed](#)]
39. Calder, P.C. Very Long-Chain n-3 Fatty Acids and Human Health: Fact, Fiction and the Future. *Proc. Nutr. Soc.* **2018**, *77*, 52–72. [[CrossRef](#)] [[PubMed](#)]
40. Yannakopoulos, A.; Tserveni-Gousi, A.; Christaki, E. Enhanced Egg Production in Practice: The Case of Bio-Omega-3 Egg. *Int. J. Poult. Sci.* **2005**, *4*, 531–535.
41. Tang, A.B.; Nishimura, K.Y.; Phinney, S.D. Preferential Reduction in Adipose Tissue α -Linolenic Acid (18:3 n-3) During Very Low Calorie Dieting Despite Supplementation with 18:3 n-3. *Lipids* **1993**, *28*, 987–993. [[CrossRef](#)]
42. Scientific Opinion on Dietary Reference Values for Fats, Including Saturated Fatty Acids, Polyunsaturated Fatty Acids, Monounsaturated Fatty Acids, Trans Fatty Acids, and Cholesterol. *EFSA J.* **2010**, *8*, 1461.
43. Helland, I.B.; Smith, L.; Saarem, K.; Saugstad, O.D.; Drevon, C.A. Maternal Supplementation with Very-Long-Chain n-3 Fatty Acids During Pregnancy and Lactation Augments Children’s IQ at 4 Years of Age. *Pediatrics* **2003**, *111*, e39–e44. [[CrossRef](#)] [[PubMed](#)]
44. Leyrolle, Q.; Decoeur, F.; Briere, G.; Amadiou, C.; Quadros, A.R.A.A.; Voytyuk, I.; Lacabanne, C.; Benmamar-Badel, A.; Bourel, J.; Aubert, A.; et al. Maternal dietary omega-3 deficiency worsens the deleterious effects of prenatal inflammation on the gut-brain axis in the offspring across lifetime. *Neuropsychopharmacology* **2021**, *46*, 579–602. [[CrossRef](#)] [[PubMed](#)]
45. Hoffman, M.C.; Freedman, R.; Law, A.J.; Clark, A.M.; Hunter, S.K. Maternal nutrients and effects of gestational COVID-19 infection on fetal brain development. *Clin. Nutr. ESPEN* **2021**, *43*, 1–8. [[CrossRef](#)]
46. Castro-Gómez, P.; Garcia-Serrano, A.; Visioli, F.; Fontecha, J. Relevance of dietary glycerophospholipids and sphingolipids to human health. *Prostaglandins Leukot. Essent. Fat. Acids* **2015**, *101*, 41–51. [[CrossRef](#)] [[PubMed](#)]
47. Aryal, S.; Hussain, S.; Drevon, C.A.; Nagelhus, E.; Hvalby, D.; Jensen, V.; Walaas, S.I.; Davanger, S. Omega-3 fatty acids regulate plasticity in distinct hippocampal glutamatergic synapses. *Eur. J. Neurosci.* **2019**, *49*, 40–50. [[CrossRef](#)] [[PubMed](#)]
48. Butler, M.; Nelson, V.A.; Davila, H.; Ratner, E.; Fink, H.A.; Hemmy, L.S.; McCarten, J.R.; Barclay, T.R.; Brasure, M.; Kane, R.L. Over-the-Counter Supplement Interventions to Prevent Cognitive Decline, Mild Cognitive Impairment, and Clinical Alzheimer-Type Dementia. *Ann. Intern. Med.* **2018**, *168*, 52–62. [[CrossRef](#)]
49. Moore, K.; Hughes, C.F.; Ward, M.; Hoey, L.; McNulty, H. Diet, Nutrition and the Ageing Brain: Current Evidence and New Directions. *Proc. Nutr. Soc.* **2018**, *77*, 152–163. [[CrossRef](#)]
50. Chew, E.Y.; Clemons, T.E.; Agrón, E.; Launer, L.J.; Grodstein, F.; Bernstein, P.S. Effect of Omega-3 Fatty Acids, Lutein/Zeaxanthin, or Other Nutrient Supplementation on Cognitive Function: The AREDS2 Randomized Clinical Trial. *JAMA J. Am. Med. Assoc.* **2015**, *314*, 791–801. [[CrossRef](#)]
51. Wood, A.H.R.; Chappell, H.F.; Zulyniak, M.A. Dietary and Supplemental Long-Chain Omega-3 Fatty Acids as Moderators of Cognitive Impairment and Alzheimer’s Disease. *Eur. J. Nutr.* **2022**, *61*, 589–604. [[CrossRef](#)]
52. Bernasconi, A.A.; Wiest, M.M.; Lavie, C.J.; Milani, R.V.; Laukkanen, J.A. Effect of Omega-3 Dosage on Cardiovascular Outcomes: An Updated Meta-Analysis and Meta-Regression of Interventional Trials. *Mayo Clin. Proc.* **2021**, *96*, 304–313. [[CrossRef](#)]
53. U.S. Food and Drug Administration (FDA) Advice about Eating Fish. Available online: <https://www.fda.gov/food/consumers/advice-about-eating-fish> (accessed on 25 January 2022).
54. Meyer, B.J.; de Groot, R.H.M. Effects of Omega-3 Long Chain Polyunsaturated Fatty Acid Supplementation on Cardiovascular Mortality: The Importance of the Dose of DHA. *Nutrients* **2017**, *9*, 1305. [[CrossRef](#)] [[PubMed](#)]
55. Van der Wurff, I.S.M.; Meyer, B.J.; de Groot, R.H.M. Effect of Omega-3 Long Chain Polyunsaturated Fatty Acids (N-3 LCPUFA) Supplementation on Cognition in Children and Adolescents: A Systematic Literature Review with a Focus on n-3 LCPUFA Blood Values and Dose of DHA and EPA. *Nutrients* **2020**, *12*, 3115. [[CrossRef](#)] [[PubMed](#)]
56. Scientific Opinion on the Tolerable Upper Intake Level of Eicosapentaenoic Acid (EPA), Docosahexaenoic Acid (DHA) and Docosapentaenoic Acid (DPA). *EFSA J.* **2012**, *10*, 2815.
57. Poulos, A.; Darin-Bennett, A.; White, I. The phospholipid-bound fatty acids and aldehydes of mammalian spermatozoa. *Comp. Biochem. Physiol. Part B Comp. Biochem.* **1973**, *46*, 541–549. [[CrossRef](#)]
58. Rodríguez, M.; Rebollar, P.G.; Mattioli, S.; Castellini, C. N-3 PUFA Sources (Precursor/Products): A Review of Current Knowledge on Rabbit. *Animals* **2019**, *9*, 806. [[CrossRef](#)]
59. Signorini, C.; Moretti, E.; Noto, D.; Mattioli, S.; Castellini, C.; Pascarelli, N.A.; Durand, T.; Oger, C.; Galano, J.M.; de Felice, C.; et al. F4-Neuroprostanes: A Role in Sperm Capacitation. *Life* **2021**, *11*, 655. [[CrossRef](#)]
60. Yuxin, L.; Chen, L.; Xiaoxia, L.; Yue, L.; Junjie, L.; Youzhu, L.; Huiliang, Z.; Qicai, L. Research Progress on the Relationship between Obesity-Inflammation-Aromatase Axis and Male Infertility. *Oxid. Med. Cell. Longev.* **2021**, *2021*, 6612796. [[CrossRef](#)]

61. Agarwal, A.; Parekh, N.; Selvam, M.K.P.; Henkel, R.; Shah, R.; Homa, S.T.; Ramasamy, R.; Ko, E.; Tremellen, K.; Esteves, S.; et al. Male Oxidative Stress Infertility (MOSI): Proposed Terminology and Clinical Practice Guidelines for Management of Idiopathic Male Infertility. *World J. Men's Health* **2019**, *37*, 296–312. [CrossRef]
62. Simopoulos, A.P. An Increase in the Omega-6/Omega-3 Fatty Acid Ratio Increases the Risk for Obesity. *Nutrients* **2016**, *8*, 128. [CrossRef]
63. Chaves, H.; Singh, R.B.; Khan, S.; Wilczynska, A.; Takahashi, T. High Omega-6/Omega-3 Fatty Acid Ratio Diets and Risk of Noncommunicable Diseases: Is the Tissue, the Main Issue? In *The Role of Functional Food Security in Global Health*, 1st ed.; Watson, R.R., Singh, R.B., Takahashi, T., Eds.; Academic Press: London, UK, 2018; pp. 217–259.
64. World Population Prospect: The 2019 Revision—United Nations, Department of Economic and Social Affairs, Population Division (June 2019). Available online: <https://population.un.org/wpp> (accessed on 26 January 2022).
65. International Programs Center at the U.S. Census Bureau, Population Division. Available online: <https://www.census.gov/programs-surveys/international-programs.html> (accessed on 29 January 2022).
66. Salem, N.; Eggersdorfer, M. Is the World Supply of Omega-3 Fatty Acids Adequate for Optimal Human Nutrition? *Curr. Opin. Clin. Nutr. Metab. Care* **2015**, *18*, 147–154. [CrossRef]
67. Cherif, A.; Dubacq, J.; Mache, R.; Oursel, A.; Tremolieres, A. Biosynthesis of α -Linolenic Acid by Desaturation of Oleic and Linoleic Acids in Several Organs of Higher and Lower Plants and in Algae. *Phytochemistry* **1975**, *14*, 703–706. [CrossRef]
68. Anai, T.; Yamada, T.; Kinoshita, T.; Rahman, S.M.; Takagi, Y. Identification of Corresponding Genes for Three Low- α -Linolenic Acid Mutants and Elucidation of Their Contribution to Fatty Acid Biosynthesis in Soybean Seed. *Plant Sci.* **2005**, *168*, 1615–1623. [CrossRef]
69. Somerville, C.; Browse, J. Plant Lipids: Metabolism, Mutants, and Membranes. *Science* **1991**, *252*, 80–87. [CrossRef] [PubMed]
70. Harwood, J.L. Fatty acid metabolism. *Annu. Rev. Plant Physiol. Plant Mol. Biol.* **1988**, *39*, 101–138. [CrossRef]
71. Harwood, J.L. Recent advances in the biosynthesis of plant fatty acids. *Biochim. Biophys. Acta (BBA)-Lipids Lipid. Metab.* **1996**, *1301*, 7–56. [CrossRef]
72. Millar, A.A.; Wrischer, M.; Kunst, L. Accumulation of Very-Long-Chain Fatty Acids in Membrane Glycerolipids Is Associated with Dramatic Alterations in Plant Morphology. *Plant Cell* **1998**, *10*, 1889–1902. [CrossRef]
73. Spychalla, J.P.; Kinney, A.J.; Browse, J. Identification of an Animal-3 Fatty Acid Desaturase by Heterologous Expression in Arabidopsis. *Proc. Natl. Acad. Sci. USA* **1997**, *94*, 1142–1147. [CrossRef]
74. Arao, T.; Yamada, M. Biosynthesis of Polyunsaturated Fatty Acids in the Marine Diatom, *Phaeodactylum Tricornutum*. *Phytochemistry* **1994**, *35*, 1177–1181. [CrossRef]
75. Arao, T.; Sakaki, T.; Yamada, M. Biosynthesis of Polyunsaturated Lipids in the Diatom, *Phaeodactylum Tricornutum*. *Phytochemistry* **1994**, *36*, 629–635. [CrossRef]
76. Bajpai, P.; Bajpai, P.K. Eicosapentaenoic Acid (EPA) Production from Microorganisms: A Review. *J. Biotechnol.* **1993**, *30*, 161–183. [CrossRef]
77. Girke, T.; Schmidt, H.; Zä Hringer, U.; Reski, R.; Heinz, E. Identification of a novel D6-acyl-group desaturase by targeted gene disruption in *Physcomitrella patens*. *Plant J.* **1998**, *15*, 39–48. [CrossRef] [PubMed]
78. Twining, C.W.; Brenna, J.T.; Hairston, N.G.; Flecker, A.S. Highly Unsaturated Fatty Acids in Nature: What We Know and What We Need to Learn. *Oikos* **2016**, *125*, 749–760. [CrossRef]
79. Twining, C.W.; Parmar, T.P.; Mathieu-Resuge, M.; Kainz, M.J.; Shipley, J.R.; Martin-Creuzburg, D. Use of Fatty Acids from Aquatic Prey Varies with Foraging Strategy. *Front. Ecol. Evol.* **2021**, *9*, 735350. [CrossRef]
80. Gill, I.; Valiveth, R. Polyunsaturated Fatty Acids, Part 1: Occurrence, Biological Activities and Applications. *Trends Biotechnol.* **1997**, *15*, 401–409. [CrossRef]
81. Gunstone, F.D. Gammar linolenic acid occurrence and physical and chemical properties. *Prog. Lipid Res.* **1992**, *31*, 145–161. [CrossRef]
82. Gunstone, F. Movements towards tailor-made fats. *Prog. Lipid Res.* **1998**, *37*, 277–305. [CrossRef]
83. US Department of Agriculture. National Nutrient Database. Available online: <http://www.nal.usda.gov/fnic/foodcomp/search/> (accessed on 25 January 2022).
84. Gebauer, S.K.; Psota, T.L.; Harris, W.S.; Kris-Etherton, P.M. N-3 Fatty Acid Dietary Recommendations and Food Sources to Achieve Essentiality and Cardiovascular Benefits. *Am. J. Clin. Nutr.* **2006**, *83*, 1526S–1535S. [CrossRef]
85. Hardy, R.W. Utilization of Plant Proteins in Fish Diets: Effects of Global Demand and Supplies of Fishmeal. *Aquac. Res.* **2010**, *41*, 770–776. [CrossRef]
86. Tocher, D.R. Metabolism and Functions of Lipids and Fatty Acids in Teleost Fish. *Rev. Fish. Sci.* **2003**, *11*, 107–184. [CrossRef]
87. Bell, M.V.; Tocher, D.R. Biosynthesis of Polyunsaturated Fatty Acids in Aquatic Ecosystems: General Pathways and New Directions. In *Lipids in Aquatic Ecosystems*, 1st ed.; Kainz, M., Brett, M., Arts, M., Eds.; Springer: New York, NY, USA, 2009; pp. 211–236.
88. Castro, L.F.C.; Tocher, D.R.; Monroig, O. Long-chain polyunsaturated fatty acid biosynthesis in chordates: Insights into the evolution of Fads and Elovl gene repertoire. *Prog. Lipid Res.* **2016**, *62*, 25–40. [CrossRef]
89. Lopes-Marques, M.; Kabeya, N.; Qian, Y.; Ruivo, R.; Santos, M.M.; Venkatesh, B.; Tocher, D.R.; Castro, L.F.C.; Monroig, Ó. Retention of Fatty Acyl Desaturase 1 (Fads1) in Elopomorpha and Cyclostomata Provides Novel Insights into the Evolution of Long-Chain Polyunsaturated Fatty Acid Biosynthesis in Vertebrates. *BMC Evol. Biol.* **2018**, *18*, 157. [CrossRef]

90. Betancor, M.B.; Oboh, A.; Ortega, A.; Mourente, G.; Navarro, J.C.; de la Gándara, F.; Tocher, D.R.; Monroig, Ó. Molecular and Functional Characterisation of a Putative Elovl4 Gene and Its Expression in Response to Dietary Fatty Acid Profile in Atlantic Bluefin Tuna (*Thunnus ihynnus*). *Comp. Biochem. Physiol. Part B Biochem. Mol. Biol.* **2020**, *240*, 110372. [[CrossRef](#)] [[PubMed](#)]
91. Hu, Q.; Sommerfeld, M.; Jarvis, E.; Ghirardi, M.; Posewitz, M.; Seibert, M.; Darzins, A. Microalgal Triacylglycerols as Feedstocks for Biofuel Production: Perspectives and Advances. *Plant J.* **2008**, *54*, 621–639. [[CrossRef](#)] [[PubMed](#)]
92. Lang, I.; Hodac, L.; Friedl, T.; Feussner, I. Fatty Acid Profiles and Their Distribution Patterns in Microalgae: A Comprehensive Analysis of More than 2000 Strains from the SAG Culture Collection. *BMC Plant Biol.* **2011**, *11*, 124. [[CrossRef](#)] [[PubMed](#)]
93. Ishikawa, A.; Kabeya, N.; Ikeya, K.; Kakioka, R.; Cech, J.N.; Osada, N.; Leal, M.C.; Inoue, J.; Kume, M.; Toyoda, A.; et al. A Key Metabolic Gene for Recurrent Freshwater Colonization and Radiation in Fishes. *Science* **2019**, *364*, 886–889. [[CrossRef](#)] [[PubMed](#)]
94. Kriton, G.; Dimitra, K.; Corraze, G.; Jaume, P.-S.; Adorjan, A.; Zsuzsanna, J.S. Impact of Diets Containing Plant Raw Materials as Fish Meal and Fish Oil Replacement on Rainbow Trout (*Oncorhynchus mykiss*), Gilthead Sea Bream (*Sparus aurata*), and Common Carp (*Cyprinus carpio*) Freshness. *J. Food Qual.* **2018**, *2018*, 1717465. [[CrossRef](#)]
95. Faudzi, N.M.; Yong, A.S.K.; Shapawi, R.; Senoo, S.; Biswas, A.; Takii, K. Soy protein concentrate as an alternative in replacement of fish meal in the feeds of hybrid grouper, brown-marbled grouper (*Epinephelus fuscoguttatus*) × giant grouper (*E. lanceolatus*) juvenile. *Aquac. Res.* **2017**, *49*, 431–441. [[CrossRef](#)]
96. Braña, C.B.C.; Cerbule, K.; Senff, P.; Stolz, I.K. Towards Environmental Sustainability in Marine Finfish Aquaculture. *Front. Mar. Sci.* **2021**, *8*. [[CrossRef](#)]
97. Hites, R.A.; Foran, J.A.; Carpenter, D.O.; Hamilton, M.C.; Knuth, B.A.; Schwager, S.J. Global Assessment of Organic Contaminants in Farmed Salmon. *Science* **2004**, *303*, 226–229. [[CrossRef](#)]
98. Thomsen, S.T.; Assunção, R.; Afonso, C.; Boué, G.; Cardoso, C.; Cubadda, F.; Garre, A.; Kruisselbrink, J.W.; Mantovani, A.; Pitter, J.G.; et al. Human Health Risk–Benefit Assessment of Fish and Other Seafood: A Scoping Review. *Crit. Rev. Food Sci. Nutr.* **2021**, 1–22. [[CrossRef](#)]
99. Adams, K.J.; Drenner, R.W.; Chumchal, M.M.; Donato, D.I. Disparity between State Fish Consumption Advisory Systems for Methylmercury and US Environmental Protection Agency Recommendations: A Case Study of the South Central United States. *Environ. Toxicol. Chem.* **2016**, *35*, 247–251. [[CrossRef](#)] [[PubMed](#)]
100. U.S. Environmental Protection Agency. Guidance for assessing chemical contaminant data for use in fish advisories. *Risk Assess. Fish Consum. Limits* **2000**, *2*.
101. Kuipers, R.S.; Luxwolda, M.F.; Offringa, P.J.; Boersma, E.R.; Dijck-Brouwer, D.J.; Muskiet, F.A. Gestational age dependent changes of the fetal brain, liver and adipose tissue fatty acid compositions in a population with high fish intakes. *Prostaglandins Leukot. Essent. Fat. Acids* **2012**, *86*, 189–199. [[CrossRef](#)] [[PubMed](#)]
102. Extier, A.; Langelier, B.; Perruchot, M.-H.; Guesnet, P.; Van Veldhoven, P.P.; Lavialle, M.; Alessandri, J.-M. Gender affects liver desaturase expression in a rat model of n–3 fatty acid repletion. *J. Nutr. Biochem.* **2010**, *21*, 180–187. [[CrossRef](#)]
103. Burdge, G.; Slater-Jefferies, J.; Grant, R.; Chung, W.-S.; West, A.; Lillycrop, K.; Hanson, M.; Calder, P. Sex, but not maternal protein or folic acid intake, determines the fatty acid composition of hepatic phospholipids, but not of triacylglycerol, in adult rats. *Prostaglandins Leukot. Essent. Fat. Acids* **2008**, *78*, 73–79. [[CrossRef](#)]
104. Toral, P.G.; Monahan, F.J.; Hervás, G.; Frutos, P.; Moloney, A.P. Review: Modulating ruminal lipid metabolism to improve the fatty acid composition of meat and milk. Challenges and opportunities. *Animal* **2018**, *12*, s272–s281. [[CrossRef](#)]
105. Ibrahim, N.A.; Alimon, A.R.; Yaakub, H.; Samsudin, A.A.; Candyryne, S.C.L.; Wan Mohamed, W.N.; Md Noh, A.; Fuat, M.A.; Mookiah, S. Effects of Vegetable Oil Supplementation on Rumen Fermentation and Microbial Population in Ruminant: A Review. *Trop. Anim. Health Prod.* **2021**, *53*, 422. [[CrossRef](#)]
106. Scislawski, V.; Bauchart, D.; Gruffat, D.; Laplaud, P.M.; Durand, D. Effects of Dietary N-6 or n-3 Polyunsaturated Fatty Acids Protected or Not against Ruminal Hydrogenation on Plasma Lipids and Their Susceptibility to Peroxidation in Fattening Steers. *J. Anim. Sci.* **2005**, *83*, 2162–2174. [[CrossRef](#)]
107. Pereira, G.; Simões, P.; Bexiga, R.; Silva, E.; Mateus, L.; Fernandes, T.; Alves, S.P.; Bessa, R.J.B.; Lopes-da-Costa, L. Effects of Feeding Rumen-Protected Linseed Fat to Postpartum Dairy Cows on Plasma n-3 Polyunsaturated Fatty Acid Concentrations and Metabolic and Reproductive Parameters. *J. Dairy Sci.* **2022**, *105*, 361–374. [[CrossRef](#)]
108. Kitessa, S.M.; Gulati, S.K.; Simos, G.C.; Ashes, J.R.; Scott, T.W.; Fleck, E.; Wynn, P.C. Supplementation of Grazing Dairy Cows with Rumen-Protected Tuna Oil Enriches Milk Fat with n -3 Fatty Acids without Affecting Milk Production or Sensory Characteristics. *Br. J. Nutr.* **2004**, *91*, 271–277. [[CrossRef](#)]
109. Simopoulos, A.P. New products from the agri-food industry: The return of n-3 fatty acids into the food supply. *Lipids* **1999**, *34*, S297–S301. [[CrossRef](#)] [[PubMed](#)]
110. FAO (Food and Agriculture Organization of the United Nations). *Fats and Fatty Acids in Human Nutrition: Report of an Expert Consultation*; FAO Food and Nutrition: Geneva, Switzerland, 2010.
111. Givens, D.; Kliem, K.E.; Gibbs, R.A. The role of meat as a source of n–3 polyunsaturated fatty acids in the human diet. *Meat Sci.* **2006**, *74*, 209–218. [[CrossRef](#)] [[PubMed](#)]
112. Williams, A.G.; Audsley, E.; Sandars, D.L. *Determining the Environmental Burdens and Resource Use in the Production of Agricultural and Horticultural Commodities*; Defra Project Report IS0205. Available online: <http://randd.defra.gov.uk/Default.aspx> (accessed on 3 May 2022).

113. Cavani, C.; Petracci, M.; Trocino, A.; Xiccato, G. Advances in Research on Poultry and Rabbit Meat Quality. *Ital. J. Anim. Sci.* **2009**, *8* (Suppl. 2), 741–750. [[CrossRef](#)]
114. Barroeta, A. Nutritive value of poultry meat: Relationship between vitamin E and PUFA. *World's Poult. Sci. J.* **2007**, *63*, 277–284. [[CrossRef](#)]
115. Abeyrathne, E.D.N.S.; Lee, H.Y.; Ahn, D.U. Egg White Proteins and Their Potential Use in Food Processing or as Nutraceutical and Pharmaceutical Agents—A Review. *Poult. Sci.* **2013**, *92*, 3292–3299. [[CrossRef](#)] [[PubMed](#)]
116. Marcet, I.; Sáez-Orviz, S.; Rendueles, M.; Díaz, M. Egg Yolk Granules and Phosvitin. Recent Advances in Food Technology and Applications. *LWT* **2022**, *153*, 112442. [[CrossRef](#)]
117. Mattioli, S.; Dal Bosco, A.; Martino, M.; Ruggeri, S.; Marconi, O.; Sileoni, V.; Falcinelli, B.; Castellini, C.; Benincasa, P. Alfalfa and Flax Sprouts Supplementation Enriches the Content of Bioactive Compounds and Lowers the Cholesterol in Hen Egg. *J. Funct. Foods* **2016**, *22*, 454–462. [[CrossRef](#)]
118. Lee, S.H.; Kim, Y.B.; Kim, D.H.; Lee, D.W.; Lee, H.G.; Jha, R.; Lee, K.W. Dietary Soluble Flaxseed Oils as a Source of Omega-3 Polyunsaturated Fatty Acids for Laying Hens. *Poult. Sci.* **2021**, *100*, 101276. [[CrossRef](#)]
119. Kwiecień, M.; Winiarska-Mieczan, A.; Danek-Majewska, A.; Kwiatkowska, K.; Krusiński, R. Effects of Dietary Alfalfa Protein Concentrate on Lipid Metabolism and Antioxidative Status of Serum and Composition and Fatty Acid Profile and Antioxidative Status and Dietetic Value of Muscles in Broilers. *Poult. Sci.* **2021**, *100*, 100974. [[CrossRef](#)]
120. Wilkinson, S.J. Big data for poultry—What is possible. In Proceedings of the 29th Annual Australian Poultry Science Symposium, Sydney, Australia, 4–7 February 2018.
121. Schreiner, M.; Hulan, H.W.; Razzazi-Fazeli, E.; Böhm, J.; Moreira, R.G. Effect of Different Sources of Dietary Omega-3 Fatty Acids on General Performance and Fatty Acid Profiles of Thigh, Breast, Liver and Portal Blood of Broilers. *J. Sci. Food Agric.* **2005**, *85*, 219–226. [[CrossRef](#)]
122. Chekani-Azar, S.; Shahriar, H.A.; Maheri-Sis, N.; Ahmadzadeh, A.R.; Vahdatpoor, T. Omega-3 Fatty Acids Enrichment and Organoleptic Characteristics of Broiler Meat. *Asian J. Anim. Vet. Adv.* **2008**, *3*, 62–69. [[CrossRef](#)]
123. Rizliya, V.; Mendis, E. Biological, Physical, and Chemical Properties of Fish Oil and Industrial Applications. In *Seafood Processing By-Products: Trends and Applications*, 1st ed.; Kim, S.K., Ed.; Springer: New York, NY, USA, 2013; pp. 285–313.
124. Harris, W.S. Fish Oils and Plasma Lipid and Lipoprotein Metabolism in Humans: A Critical Review. *J. Lipid Res.* **1989**, *30*, 785–807. [[CrossRef](#)]
125. Sprecher, H.W.; Baykousheva, S.P.; Luthria, D.L.; Mohammed, B.S. Differences in the Regulation of Biosynthesis of 20- versus 22-Carbon Polyunsaturated Fatty Acids. *Prostaglandins Leukot. Essent. Fat. Acids* **1995**, *52*, 99–101. [[CrossRef](#)]
126. Bonos, E.; Kasapidou, E.; Kargopoulos, A.; Karampampas, A.; Christaki, E.; Florou-Paneri, P.; Nikolakakis, I. Spirulina as a Functional Ingredient in Broiler Chicken Diets. *S. Afr. J. Anim. Sci.* **2016**, *46*, 94–102. [[CrossRef](#)]
127. Alfaia, C.M.; Pestana, J.M.; Rodrigues, M.; Coelho, D.; Aires, M.J.; Ribeiro, D.M.; Major, V.T.; Martins, C.F.; Santos, H.; Lopes, P.A.; et al. Influence of Dietary Chlorella Vulgaris and Carbohydrate-Active Enzymes on Growth Performance, Meat Quality and Lipid Composition of Broiler Chickens. *Poult. Sci.* **2021**, *100*, 926–937. [[CrossRef](#)]
128. El-Bahr, S.; Shousha, S.; Shehab, A.; Khattab, W.; Ahmed-Farid, O.; Sabike, I.; El-Garhy, O.; Albokhadaim, I.; Albosadah, K. Effect of Dietary Microalgae on Growth Performance, Profiles of Amino and Fatty Acids, Antioxidant Status, and Meat Quality of Broiler Chickens. *Animals* **2020**, *10*, 761. [[CrossRef](#)]
129. Costa, M.M.; Pestana, J.M.; Osório, D.; Alfaia, C.M.; Martins, C.F.; Mourato, M.; Gueifão, S.; Rego, A.M.; Coelho, I.; Coelho, D.; et al. Effect of Dietary Laminaria Digitata with Carbohydrases on Broiler Production Performance and Meat Quality, Lipid Profile, and Mineral Composition. *Animals* **2022**, *12*, 1007. [[CrossRef](#)]
130. Jankowski, J.; Zduńczyk, Z.; Mikulski, D.; Juśkiewicz, J.; Pomianowski, J.F.; Zduńczyk, P. Fatty Acid Profile, Oxidative Stability and Sensory Quality of Breast Meat from Turkeys Fed Diets with Graded Levels of Flaxseed Oil for Different Periods of Time. *Anim. Prod. Sci.* **2018**, *58*, 1164–1174. [[CrossRef](#)]
131. López-Ferrer, S.; Baucells, M.D.; Barroeta, A.C.; Galobart, J.; Grashorn, M.A. N-3 Enrichment of Chicken Meat. 2. Use of Precursors of Long-Chain Polyunsaturated Fatty Acids: Linseed Oil. *Poult. Sci.* **2001**, *80*, 753–761. [[CrossRef](#)]
132. Kartikasari, L.R.; Hughes, R.J.; Geier, M.S.; Makrides, M.; Gibson, R.A. Dietary Alpha-Linolenic Acid Enhances Omega-3 Long Chain Polyunsaturated Fatty Acid Levels in Chicken Tissues. *Prostaglandins Leukot. Essent. Fat. Acids* **2012**, *87*, 103–109. [[CrossRef](#)]
133. López-Ferrer, S.; Baucells, M.D.; Barroeta, A.C.; Grashorn, M.A. N-3 Enrichment of Chicken Meat Using Fish Oil: Alternative Substitution with Rapeseed and Linseed Oils. *Poult. Sci.* **1999**, *78*, 356–365. [[CrossRef](#)] [[PubMed](#)]
134. Gonzalez-Esquerria, R.; Leeson, S. Effects of Menhaden Oil and Flaxseed in Broiler Diets on Sensory Quality and Lipid Composition of Poultry Meat. *Br. Poult. Sci.* **2000**, *41*, 481–488. [[CrossRef](#)] [[PubMed](#)]
135. Zelenka, J.; Jarošová, A.; Schneiderová, D. Influence of N-3 and n-6 Polyunsaturated Fatty Acids on Sensory Characteristics of Chicken Meat. *Czech J. Anim. Sci.* **2008**, *53*, 299–305. [[CrossRef](#)]
136. Surai, P.F.; Kochish, I.I.; Romanov, M.N.; Griffin, D.K. Nutritional Modulation of the Antioxidant Capacities in Poultry: The Case of Vitamin E. *Poult. Sci.* **2019**, *98*, 4030–4041. [[CrossRef](#)]
137. González-Ortiz, G.; Sala, R.; Cánovas, E.; Abed, N.; Barroeta, A.C. Consumption of Dietary N-3 Fatty Acids Decreases Fat Deposition and Adipocyte Size, but Increases Oxidative Susceptibility in Broiler Chickens. *Lipids* **2013**, *48*, 705–717. [[CrossRef](#)]

138. Shin, D.; Choi, S.; Go, G.; Park, J.; Narciso-Gaytán, C.; Morgan, C.; Smith, S.; Sánchez-Plata, M.; Ruiz-Feria, C. Effects of dietary combination of n-3 and n-9 fatty acids on the deposition of linoleic and arachidonic acid in broiler chicken meats. *Poult. Sci.* **2012**, *91*, 1009–1017. [[CrossRef](#)]
139. Cortinas, L.; Villaverde, C.; Galobart, J.; Baucells, M.D.; Codony, R.; Barroeta, A.C. Fatty Acid Content in Chicken Thigh and Breast as Affected by Dietary Polyunsaturation Level. *Poult. Sci.* **2004**, *83*, 1155–1164. [[CrossRef](#)]
140. Rymmer, C.; Givens, D.I. Effect of Species and Genotype on the Efficiency of Enrichment of Poultry Meat with N-3 Polyunsaturated Fatty Acids. *Lipids* **2006**, *41*, 445–451. [[CrossRef](#)]
141. Brooks, G.A.; Mercier, J. Balance of Carbohydrate and Lipid Utilization during Exercise: The “crossover” Concept. *J. Appl. Physiol.* **1994**, *76*, 2253–2261. [[CrossRef](#)]
142. Schulz, H. Beta oxidation of fatty acids. *Biochim. Et Biophys. Acta (BBA) Lipids Lipid Metab.* **1991**, *1081*, 109–120. [[CrossRef](#)]
143. Cartoni Mancinelli, A.; di Veroli, A.; Mattioli, S.; Cruciani, G.; Dal Bosco, A.; Castellini, C. Lipid Metabolism Analysis in Liver of Different Chicken Genotypes and Impact on Nutritionally Relevant Polyunsaturated Fatty Acids of Meat. *Sci. Rep.* **2022**, *12*, 1888. [[CrossRef](#)] [[PubMed](#)]
144. Marra, C.A.; de Alaniz, M.J.T. Influence of Testosterone Administration on the Biosynthesis of Unsaturated Fatty Acids in Male and Female Rats. *Lipids* **1989**, *24*, 1014–1019. [[CrossRef](#)] [[PubMed](#)]
145. Burdge, G.C.; Wootton, S.A. Conversion of α -Linolenic Acid to Eicosapentaenoic, Docosapentaenoic and Docosahexaenoic Acids in Young Women. *Br. J. Nutr.* **2002**, *88*, 411–420. [[CrossRef](#)] [[PubMed](#)]
146. Poureslami, R.; Raes, K.; Turchini, G.M.; Huyghebaert, G.; de Smet, S. Effect of Diet, Sex and Age on Fatty Acid Metabolism in Broiler Chickens: N-3 and n-6 PUFA. *Br. J. Nutr.* **2010**, *104*, 189–197. [[CrossRef](#)]
147. Abedi, E.; Sahari, M.A. Long-Chain Polyunsaturated Fatty Acid Sources and Evaluation of Their Nutritional and Functional Properties. *Food Sci. Nutr.* **2014**, *2*, 443–463. [[CrossRef](#)]
148. Aymond, W.M.; VAN Elswyk, M.E. Yolk Thiobarbituric Acid Reactive Substances and n-3 Fatty Acids in Response to Whole and Ground Flaxseed. *Poult. Sci.* **1995**, *74*, 1388–1394. [[CrossRef](#)]
149. Hayat, Z.; Cherian, G.; Pasha, T.N.; Khattak, F.M.; Jabbar, M.A. Effect of feeding flax and two types of antioxidants on egg production, egg quality, and lipid composition of eggs. *J. Appl. Poult. Res.* **2009**, *18*, 541–551. [[CrossRef](#)]
150. Caston, L.J.; Squires, E.J.; Leeson, S. Hen performance, egg quality, and the sensory evaluation of eggs from SCWL hens fed dietary flax. *Can. J. Anim. Sci.* **1994**, *74*, 347–353. [[CrossRef](#)]
151. Rizzi, L.; Bochicchio, D.; Bargellini, A.; Parazza, P.; Simioli, M. Effects of dietary microalgae, other lipid sources, inorganic selenium and iodine on yolk n-3 fatty acid composition, selenium content and quality of eggs in laying hens. *J. Sci. Food Agric.* **2009**, *89*, 1775–1781. [[CrossRef](#)]
152. Bean, L.; Leeson, S. Long-term effects of feeding flaxseed on performance and egg fatty acid composition of brown and white hens. *Poult. Sci.* **2003**, *82*, 388–394. [[CrossRef](#)]
153. Mattioli, S.; Ruggeri, S.; Sebastiani, B.; Brecchia, G.; Dal Bosco, A.; Cartoni Mancinelli, A.; Castellini, C. Performance and Egg Quality of Laying Hens Fed Flaxseed: Highlights on n-3 Fatty Acids, Cholesterol, Lignans and Isoflavones. *Animal* **2017**, *11*, 705–712. [[CrossRef](#)] [[PubMed](#)]
154. Scheideler, S.E.; Jaroni, D.; Froning, G. Strain and Age Effects on Egg Composition from Hens Fed Diets Rich in N-3 Fatty Acids. *Poult. Sci.* **1998**, *77*, 192–196. [[CrossRef](#)] [[PubMed](#)]
155. Aguillón-Páez, Y.J.; Romero, L.A.; Diaz, G.J. Effect of Full-Fat Sunflower or Flaxseed Seeds Dietary Inclusion on Performance, Egg Yolk Fatty Acid Profile and Egg Quality in Laying Hens. *Anim. Nutr.* **2020**, *6*, 179–184. [[CrossRef](#)]
156. Alzueta, C.; Rodríguez, M.L.; Cutuli, M.T.; Rebolé, A.; Ortiz, L.T.; Centeno, C.; Treviño, J. Effect of Whole and Demucilaged Linseed in Broiler Chicken Diets on Digesta Viscosity, Nutrient Utilisation and Intestinal Microflora. *Br. Poult. Sci.* **2003**, *44*, 67–74. [[CrossRef](#)] [[PubMed](#)]
157. Goyal, A.; Sharma, V.; Upadhyay, N.; Gill, S.; Sihag, M. Flax and flaxseed oil: An ancient medicine & modern functional food. *J. Food Sci. Technol.* **2014**, *51*, 1633–1653. [[CrossRef](#)] [[PubMed](#)]
158. Imran, M.; Anjum, F.M.; Nadeem, M.; Ahmad, N.; Khan, M.K.; Mushtaq, Z.; Hussain, S. Production of Bio-Omega-3 Eggs through the Supplementation of Extruded Flaxseed Meal in Hen Diet. *Lipids Health Dis.* **2015**, *14*, 126. [[CrossRef](#)] [[PubMed](#)]
159. Huang, S.; Baurhoo, B.; Mustafa, A. Effects of Feeding Extruded Flaxseed on Layer Performance, Total Tract Nutrient Digestibility, and Fatty Acid Concentrations of Egg Yolk, Plasma and Liver. *J. Anim. Physiol. Anim. Nutr.* **2020**, *104*, 1365–1374. [[CrossRef](#)]
160. Westbrook, L.A.; Cherian, G. Egg Quality, Fatty-Acid Composition and Gastrointestinal Morphology of Layer Hens Fed Whole Flaxseed with Enzyme Supplementation. *Br. Poult. Sci.* **2019**, *60*, 146–153. [[CrossRef](#)]
161. Kralik, G.; Kralik, Z.; Grčević, M.; Galović, O.; Hanžek, D.; Biazik, E. Fatty Acid Profile of Eggs Produced by Laying Hens Fed Diets Containing Different Shares of Fish Oil. *Poult. Sci.* **2021**, *100*, 101379. [[CrossRef](#)]
162. Beynen, A.C. Fatty Acid Composition of Eggs Produced by Hens Fed Diets Containing Groundnut, Soya Bean or Linseed. *NJAS Wagening. J. Life Sci.* **2004**, *52*, 3–10. [[CrossRef](#)]
163. Jiang, Z.R.; Ahn, D.U.; Sim, J.S. Effects of Feeding Flax and Two Types of Sunflower Seeds on Fatty Acid Compositions of Yolk Lipid Classes. *Poult. Sci.* **1991**, *70*, 2467–2475. [[CrossRef](#)] [[PubMed](#)]
164. Fraeye, I.; Bruneel, C.; Lemahieu, C.; Buyse, J.; Muylaert, K.; Foubert, I. Dietary Enrichment of Eggs with Omega-3 Fatty Acids: A Review. *Food Res. Int.* **2012**, *48*, 961–969. [[CrossRef](#)]

165. Irawan, A.; Ningsih, N.; Hafizuddin; Rusli, R.K.; Suprayogi, W.P.S.; Akhirini, N.; Hadi, R.F.; Setyono, W.; Jayanegara, A. Supplementary N-3 Fatty Acids Sources on Performance and Formation of Omega-3 in Egg of Laying Hens: A Meta-Analysis. *Poult. Sci.* **2022**, *101*, 101566. [[CrossRef](#)] [[PubMed](#)]
166. Huang, S.; Baurhoo, B.; Mustafa, A. Effects of Extruded Flaxseed on Layer Performance, Nutrient Retention and Yolk Fatty Acid Composition. *Br. Poult. Sci.* **2018**, *59*, 463–469. [[CrossRef](#)] [[PubMed](#)]
167. Omri, B.; Chalghoumi, R.; Izzo, L.; Ritieni, A.; Lucarini, M.; Durazzo, A.; Abdouli, H.; Santini, A. Effect of Dietary Incorporation of Linseed Alone or Together with Tomato-Red Pepper Mix on Laying Hens' Egg Yolk Fatty Acids Profile and Health Lipid Indexes. *Nutrients* **2019**, *11*, 813. [[CrossRef](#)] [[PubMed](#)]
168. Grobas, S.; Mateos, G.G.; Mendez, J. Influence of Dietary Linoleic Acid on Production and Weight of Eggs and Egg Components in Young Brown Hens. *J. Appl. Poult. Res.* **1999**, *8*, 177–184. [[CrossRef](#)]
169. Dong, X.; Liu, S.; Tong, J. Comparative Effect of Dietary Soybean Oil, Fish Oil, and Coconut Oil on Performance, Egg Quality and Some Blood Parameters in Laying Hens. *Poult. Sci.* **2018**, *97*, 2460–2472. [[CrossRef](#)]
170. Meluzzi, A.; Sirri, F.; Castellini, C.; Roncarati, A.; Melotti, P.; Franchini, A. Influence of genotype and feeding on chemical composition of organic chicken meat. *Ital. J. Anim. Sci.* **2009**, *8*, 766–768. [[CrossRef](#)]
171. Mugnai, C.; Sossidou, E.N.; Bosco, A.D.; Ruggeri, S.; Mattioli, S.; Castellini, C. The effects of husbandry system on the grass intake and egg nutritive characteristics of laying hens. *J. Sci. Food Agric.* **2014**, *94*, 459–467. [[CrossRef](#)]
172. Hallmann, C.A.; Sorg, M.; Jongejans, E.; Siepel, H.; Hofland, N.; Schwan, H.; Stenmans, W.; Müller, A.; Sumser, H.; Hörrn, T.; et al. More than 75 percent decline over 27 years in total flying insect biomass in protected areas. *PLoS ONE* **2017**, *12*, e0185809. [[CrossRef](#)]
173. Fanatico, A.C.; Arsi, K.; Upadhyaya, I.; Ramos, J.M.; Donoghue, D.; Donoghue, A.M. Sustainable Fish and Invertebrate Meals for Methionine and Protein Feeds in Organic Poultry Production. *J. Appl. Poult. Res.* **2018**, *27*, 437–448. [[CrossRef](#)]
174. van der Heide, M.E.; Stødkilde, L.; Nørgaard, J.V.; Studnitz, M. The Potential of Locally-Sourced European Protein Sources for Organic Monogastric Production: A Review of Forage Crop Extracts, Seaweed, Starfish, Mussel, and Insects. *Sustainability* **2021**, *13*, 2303. [[CrossRef](#)]
175. Bessa, L.W.; Pieterse, E.; Marais, J.; Hoffman, L.C. Why for feed and not for human consumption? The black soldier fly larvae. *Compr. Rev. Food Sci. Food Saf.* **2020**, *19*, 2747–2763. [[CrossRef](#)] [[PubMed](#)]
176. Caligiani, A.; Marseglia, A.; Sorci, A.; Bonzanini, F.; Lolli, V.; Maistrello, L.; Sforza, S. Influence of the killing method of the black soldier fly on its lipid composition. *Food Res. Int.* **2019**, *116*, 276–282. [[CrossRef](#)]
177. Liu, X.; Chen, X.; Wang, H.; Yang, Q.; Ur Rehman, K.; Li, W.; Cai, M.; Li, Q.; Mazza, L.; Zhang, J.; et al. Dynamic Changes of Nutrient Composition throughout the Entire Life Cycle of Black Soldier Fly. *PLoS ONE* **2017**, *12*, e0182601. [[CrossRef](#)]
178. Finke, M.D.; Oonincx, D.G.A.B. Nutrient Content of Insects. In *Insects as Food and Feed: From Production to Consumption*; van Huis, A., Tomberlin, J.K., Eds.; Wageningen Academic Publishers: Wageningen, The Netherlands, 2016; pp. 290–316.
179. Sánchez-Muros, M.-J.; Barroso, F.; Manzano-Agugliaro, F. Insect meal as renewable source of food for animal feeding: A review. *J. Clean. Prod.* **2014**, *65*, 16–27. [[CrossRef](#)]
180. Bbosa, T.; Ndagire, C.T.; Mukisa, I.M.; Fiaboe, K.K.M.; Nakimbugwe, D. Nutritional Characteristics of Selected Insects in Uganda for Use as Alternative Protein Sources in Food and Feed. *J. Insect Sci.* **2019**, *19*, 23. [[CrossRef](#)]
181. Schreven, S.; Yener, S.; Van Valenberg, H.; Dicke, M.; Van Loon, J. Life on a piece of cake: Performance and fatty acid profiles of black soldier fly larvae fed oilseed by-products. *J. Insects Food Feed* **2021**, *7*, 35–49. [[CrossRef](#)]
182. Hoc, B.; Genva, M.; Fauconnier, M.-L.; Lognay, G.; Francis, F.; Megido, R.C. About lipid metabolism in *Hermetia illucens* (L. 1758): On the origin of fatty acids in prepupae. *Sci. Rep.* **2020**, *10*, 11916. [[CrossRef](#)]
183. Rossi, G.; Mattioli, S.; Rondoni Rondoni, G.; Dal Bosco, A.; Servili, M. Characterisation of Fatty Acid Profiles of *Tenebrio Molitor* Larvae Reared on Diets Enriched with Edible Oils. *J. Insects Food Feed.* **2022**, 1–12. [[CrossRef](#)]
184. Kierończyk, B.; Rawski, M.; Józefiak, A.; Mazurkiewicz, J.; Świątkiewicz, S.; Siwek, M.; Bednarczyk, M.; Szumacher-Strabel, M.; Cieślak, A.; Benzertiha, A.; et al. Effects of Replacing Soybean Oil with Selected Insect Fats on Broilers. *Anim. Feed. Sci. Technol.* **2018**, *240*, 170–183. [[CrossRef](#)]
185. Schiavone, A.; Cullere, M.; de Marco, M.; Meneguz, M.; Biasato, I.; Bergagna, S.; Dezzutto, D.; Gai, F.; Dabbou, S.; Gasco, L.; et al. Partial or Total Replacement of Soybean Oil by Black Soldier Fly Larvae (*Hermetia Illucens* L.) Fat in Broiler Diets: Effect on Growth Performances, Feed-Choice, Blood Traits, Carcass Characteristics and Meat Quality. *Ital. J. Anim. Sci.* **2017**, *16*, 93–100. [[CrossRef](#)]
186. Premalatha, M.; Abbasi, T.; Abbasi, T.; Abbasi, S.A. Energy-Efficient Food Production to Reduce Global Warming and Ecodegradation: The Use of Edible Insects. *Renew. Sustain. Energy Rev.* **2011**, *15*, 4357–4360. [[CrossRef](#)]
187. Schiavone, A.; Dabbou, S.; de Marco, M.; Cullere, M.; Biasato, I.; Biasibetti, E.; Capucchio, M.T.; Bergagna, S.; Dezzutto, D.; Meneguz, M.; et al. Black Soldier Fly Larva Fat Inclusion in Finisher Broiler Chicken Diet as an Alternative Fat Source. *Animal* **2018**, *12*, 2032–2039. [[CrossRef](#)]
188. Barroso, F.G.; Sánchez-Muros, M.J.; Segura, M.; Morote, E.; Torres, A.; Ramos, R.; Guil, J.L. Insects as Food: Enrichment of Larvae of *Hermetia Illucens* with Omega 3 Fatty Acids by Means of Dietary Modifications. *J. Food Compos. Anal.* **2017**, *62*, 8–13. [[CrossRef](#)]
189. Oonincx, D.G.A.B.; Laurent, S.; Veenbos, M.E.; van Loon, J.J.A. Dietary Enrichment of Edible Insects with Omega 3 Fatty Acids. *Insect Sci.* **2020**, *27*, 500–509. [[CrossRef](#)]

190. Oonincx, D.G.A.B.; Finke, M.D. Nutritional Value of Insects and Ways to Manipulate Their Composition. *J. Insects Food Feed.* **2021**, *7*, 639–659. [CrossRef]
191. Liland, N.S.; Biancarosa, I.; Araujo, P.; Biemans, D.; Bruckner, C.G.; Waagbø, R.; Torstensen, B.E.; Lock, E.J. Modulation of Nutrient Composition of Black Soldier Fly (*Hermetia illucens*) Larvae by Feeding Seaweed-Enriched Media. *PLoS ONE* **2017**, *12*, e0183188. [CrossRef]
192. St-Hilaire, S.; Cranfill, K.; McGuire, M.A.; Mosley, E.E.; Tomberlin, J.K.; Newton, L.; Sealey, W.; Sheppard, C.; Irving, S. Fish Offal Recycling by the Black Soldier Fly Produces a Foodstuff High in Omega-3 Fatty Acids. *J. World Aquac. Soc.* **2007**, *38*, 309–313. [CrossRef]
193. Ding, S.; Lin, X.; He, S. Earthworms: A source of protein. *J. Food Sci. Eng.* **2019**, *9*, 159–170.
194. Sampedro, L.; Jeannotte, R.; Whalen, J.K. Trophic Transfer of Fatty Acids from Gut Microbiota to the Earthworm *Lumbricus terrestris* L. *Soil Biol. Biochem.* **2006**, *38*, 2188–2198. [CrossRef]
195. Khan, S.; Naz, S.; Sultan, A.; Alhidary, I.; Abdelrahman, M.; Khan, R.; Khan, N.; Khan, M.; Ahmad, S. Worm meal: A potential source of alternative protein in poultry feed. *World's Poultry Sci. J.* **2016**, *72*, 93–102. [CrossRef]
196. Prayogi, H.S. The Effect of Earthworm Meal Supplementation in the Diet on Quail's Growth Performance in Attempt to Replace the Usage of Fish Meal. *Int. J. Poultry Sci.* **2011**, *10*, 804–806. [CrossRef]
197. Rezaei-pour, V.; Nejad, O.A.; Miri, H.Y. Growth Performance, Blood Metabolites and Jejunum Morphology of Broiler Chickens Fed Diets Containing Earthworm (*Eisenia foetida*) Meal as a Source of Protein. *Int. J. Adv. Biol. Biomed. Res.* **2014**, *2*, 2483–2494.
198. Son, J.H. The study on treatment of poultry waste by earthworms, and the effect of feeding earthworms meal on the performance of broilers and laying hens, and safety of meat and egg. *Korean J. Org. Agric.* **2009**, *17*, 17–63.
199. Son, J.H.; Jo, I.H. Effects of Earthworm Meal Supplementation on the Performance of Broiler Chickens. *Korean J. Org. Agric.* **2003**.
200. Zang, Y.T.; Bing, S.; Zhang, Y.Z.; Sheng, X.W.; Shu, D.Q. Effects of Dietary Supplementation with Earthworm Powder on Production Performance, Blood Characteristics, and Heavy Metal Residues of Broiler Pullets. *J. Appl. Poultry Res.* **2018**, *27*, 609–615. [CrossRef]
201. Isea-León, F.; Acosta-Balbás, V.; Beatriz Rial-Betancout, L.; Luisa Medina-Gallardo, A.; Mélécony Célestin, B. Evaluation of the Fatty Acid Composition of Earthworm *Eisenia andrei* Meal as an Alternative Lipid Source for Fish Feed. *J. Food Nutr. Res.* **2019**, *7*, 696–700. [CrossRef]
202. EU Commission. Commission Regulation (EU) No. 68/2013 on the Catalogue of Feed Materials. Available online: <https://www.ecolex.org/details/legislation/commission-regulation-eu-no-682013-on-the-catalogue-of-feed-materials-lex-faoc119700/> (accessed on 10 February 2022).
203. Cartoni Mancinelli, A.; Franzoni, A.; Dal Bosco, A.; Schiavone, A.; Mannelli, F.; Marzoni, M.; Castellini, C. Distribution and Consistency of Ancona and Livorno Poultry Breed in Central Italy. *Ital. J. Anim. Sci.* **2020**, *19*, 1297–1303. [CrossRef]
204. Mancinelli, A.C.; Mattioli, S.; Menchetti, L.; Bosco, A.D.; Ciarelli, C.; Amato, M.G.; Castellini, C. The Assessment of a Multifactorial Score for the Adaptability Evaluation of Six Poultry Genotypes to the Organic System. *Animals* **2021**, *11*, 2992. [CrossRef]
205. Mattioli, S.; Mancinelli, A.C.; Menchetti, L.; Bosco, A.D.; Madeo, L.; Amato, M.G.; Moscati, L.; Cotozzolo, E.; Ciarelli, C.; Angelucci, E.; et al. How the kinetic behavior of organic chickens affects productive performance and blood and meat oxidative status: A study of six poultry genotypes. *Poultry Sci.* **2021**, *100*, 101297. [CrossRef]
206. Van der Waaij, E.H. A Resource Allocation Model Describing Consequences of Artificial Selection under Metabolic Stress. *J. Anim. Sci.* **2004**, *82*, 973–981. [CrossRef] [PubMed]
207. Sirri, F.; Castellini, C.; Bianchi, M.; Petracci, M.; Meluzzi, A.; Franchini, A. Effect of Fast-, Medium- and Slow-Growing Strains on Meat Quality of Chickens Reared under the Organic Farming Method. *Animal* **2011**, *5*, 312–319. [CrossRef]
208. Castellini, C.; Dal Bosco, A.; Mugnai, C.; Bernardini, M. Performance and Behaviour of Chickens with Different Growing Rate Reared According to the Organic System. *Ital. J. Anim. Sci.* **2003**, *6*, 561–573. [CrossRef]
209. Boschetti, E.; Bordoni, A.; Meluzzi, A.; Castellini, C.; Bosco, A.D.; Sirri, F. Fatty acid composition of chicken breast meat is dependent on genotype-related variation of FADS1 and FADS2 gene expression and desaturating activity. *Animal* **2016**, *10*, 700–708. [CrossRef] [PubMed]
210. Castellini, C.; Dal Bosco, A.; Mattioli, S.; Davidescu, M.; Corazzi, L.; MacChioni, L.; Rimoldi, S.; Terova, G. Activity, Expression, and Substrate Preference of the $\Delta 6$ -Desaturase in Slow- or Fast-Growing Rabbit Genotypes. *J. Agric. Food Chem.* **2016**, *64*, 792–800. [CrossRef]
211. Dal Bosco, A.; Mugnai, C.; Ruggeri, S.; Mattioli, S.; Castellini, C. Fatty Acid Composition of Meat and Estimated Indices of Lipid Metabolism in Different Poultry Genotypes Reared under Organic System. *Poultry Sci.* **2012**, *91*, 2039–2045. [CrossRef]
212. Al-Hilal, M.; AlSaleh, A.; Maniou, Z.; Lewis, F.J.; Hall, W.L.; Sanders, T.A.B.; O'Dell, S.D. Genetic Variation at the FADS1-FADS2 Gene Locus Influences Delta-5 Desaturase Activity and LC-PUFA Proportions after Fish Oil Supplement. *J. Lipid Res.* **2013**, *54*, 542–551. [CrossRef] [PubMed]
213. Poultry | European Commission. Available online: https://ec.europa.eu/info/food-farming-fisheries/animals-and-animal-products/animal-products_en (accessed on 15 February 2022).
214. Bosco, A.D.; Mattioli, S.; Mancinelli, A.C.; Cotozzolo, E.; Castellini, C. Extensive Rearing Systems in Poultry Production: The Right Chicken for the Right Farming System. A Review of Twenty Years of Scientific Research in Perugia University, Italy. *Animals* **2021**, *11*, 1281. [CrossRef]

215. Baéza, E.; Guillier, L.; Petracci, M. Review: Production factors affecting poultry carcass and meat quality attributes. *Animal* **2021**, *16*, 100331. [[CrossRef](#)]
216. Dal Bosco, A.; Mugnai, C.; Mattioli, S.; Rosati, A.; Ruggeri, S.; Ranucci, D.; Castellini, C. Transfer of bioactive compounds from pasture to meat in organic free-range chickens. *Poult. Sci.* **2016**, *95*, 2464–2471. [[CrossRef](#)]
217. Mancinelli, A.C.; Matioli, S.; Bosco, A.D.; Ciarelli, C.; Castellini, C. Grass intake and meat oxidative status of geese reared in three different agroforestry systems. *Acta Fytotech. Zootech.* **2020**, *23*, 308–315. [[CrossRef](#)]
218. Bari, S.; Cohen-Barnhouse, A.M.; Campbell, D.L.M. Early rearing enrichments influenced nest use and egg quality in free-range laying hens. *Animal* **2020**, *14*, 1249–1257. [[CrossRef](#)] [[PubMed](#)]
219. Mancinelli, A.C.; Mattioli, S.; Dal Bosco, A.; Piottoli, L.; Ranucci, D.; Branciarri, R.; Cotozzolo, E.; Castellini, C. Rearing Romagnola geese in vineyard: Pasture and antioxidant intake, performance, carcass and meat quality. *Ital. J. Anim. Sci.* **2019**, *18*, 372–380. [[CrossRef](#)]
220. Popova, T.; Petkov, E.; Ignatova, M. Fatty acid composition of breast meat in two lines of slow-growing chickens reared conventionally or on pasture. *Food Sci. Appl. Biotechnol.* **2018**, *1*, 70–76. [[CrossRef](#)]
221. Mugnai, C.; Bosco, A.D.; Castellini, C. Effect of rearing system and season on the performance and egg characteristics of Ancona laying hens. *Ital. J. Anim. Sci.* **2009**, *8*, 175–188. [[CrossRef](#)]
222. Gou, Z.; Abouelezz, K.; Fan, Q.; Li, L.; Lin, X.; Wang, Y.; Cui, X.; Ye, J.; Masoud, M.; Jiang, S.; et al. Physiological effects of transport duration on stress biomarkers and meat quality of medium-growing Yellow broiler chickens. *Animal* **2020**, *15*, 100079. [[CrossRef](#)] [[PubMed](#)]
223. Mancinelli, A.C.; Mugnai, C.; Castellini, C.; Mattioli, S.; Moscati, L.; Piottoli, L.; Amato, M.G.; Doretto, M.; Bosco, A.D.; Cordovani, E.; et al. Effect of transport length and genotype on tonic immobility, blood parameters and carcass contamination of free-range reared chickens. *Ital. J. Anim. Sci.* **2018**, *17*, 557–564. [[CrossRef](#)]
224. Rimoldi, S.; Lasagna, E.; Sarti, F.M.; Marelli, S.P.; Cozzi, M.C.; Bernardini, G.; Terova, G. Expression profile of six stress-related genes and productive performances of fast and slow growing broiler strains reared under heat stress conditions. *Meta Gene* **2015**, *6*, 17–25. [[CrossRef](#)]
225. Berri, C.; le Bihan-Duval, E.; Debut, M.; Santé-Lhoutellier, V.; Baéza, E.; Gigaud, V.; Jégo, Y.; Duclos, M.J. Consequence of Muscle Hypertrophy on Characteristics of Pectoralis Major Muscle and Breast Meat Quality of Broiler Chickens. *J. Anim. Sci.* **2007**, *85*, 2005–2011. [[CrossRef](#)]
226. Castellini, C.; Mattioli, S.; Piottoli, L.; Mancinelli, A.C.; Ranucci, D.; Branciarri, R.; Amato, M.G.; Dal Bosco, A. Effect of Transport Length on in Vivo Oxidative Status and Breast Meat Characteristics in Outdoor-Reared Chicken Genotypes. *Ital. J. Anim. Sci.* **2016**, *15*, 191–199. [[CrossRef](#)]
227. Mancinelli, A.C.; Bosco, A.D.; Mattioli, S.; Ranucci, D.; Castellini, C. Mobile Poultry Processing Unit as a Resource for Small Poultry Farms: Planning and Economic Efficiency, Animal Welfare, Meat Quality and Sanitary Implications. *Animals* **2018**, *8*, 229. [[CrossRef](#)] [[PubMed](#)]
228. Rhee, K.; Anderson, L.; Sams, A. Lipid Oxidation Potential of Beef, Chicken, and Pork. *J. Food Sci.* **1996**, *61*, 8–12. [[CrossRef](#)]
229. Amaral, A.B.; da Silva, M.V.; Lannes, S.C.D.S. Lipid oxidation in meat: Mechanisms and protective factors—A review. *Food Sci. Technol.* **2018**, *38*, 1–15. [[CrossRef](#)]
230. Bassam, S.M.; Noleto-Dias, C.; Farag, M.A. Dissecting grilled red and white meat flavor: Its characteristics, production mechanisms, influencing factors and chemical hazards. *Food Chem.* **2022**, *371*, 131139. [[CrossRef](#)] [[PubMed](#)]
231. Pearson, A.M.; Love, J.D.; Shorland, F.B. “Warmed-over” Flavor in Meat, Poultry, and Fish. *Adv. Food Res.* **1977**, *23*, 1–74.
232. Byrne, D.V.; Bredie, W.L.P.; Mottram, D.S.; Martens, M. Sensory and Chemical Investigations on the Effect of Oven Cooking on Warmed-over Flavour Development in Chicken Meat. *Meat Sci.* **2002**, *61*, 127–139. [[CrossRef](#)]
233. Mancinelli, A.C.; Silletti, E.; Mattioli, S.; Bosco, A.D.; Sebastiani, B.; Menchetti, L.; Koot, A.; van Ruth, S.; Castellini, C. Fatty acid profile, oxidative status, and content of volatile organic compounds in raw and cooked meat of different chicken strains. *Poult. Sci.* **2020**, *100*, 1273–1282. [[CrossRef](#)]
234. Mattioli, S.; Dal Bosco, A.; Ruggeri, S.; Martino, M.; Moscati, L.; Pesca, C.; Castellini, C. Adaptive Response to Exercise of Fast-Growing and Slow-Growing Chicken Strains: Blood Oxidative Status and Non-Enzymatic Antioxidant Defense. *Poult. Sci.* **2017**, *96*, 4096–4102. [[CrossRef](#)]