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Review Article

Redox Mediated Lipid Metabolism in Animals: Mechanisms and Veterinary Relevance in Companion Animals and Wild Birds

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ABSTRACT

Lipids are essential for animal physiology; however, dysregulated lipid metabolism can induce metabolic stress and impair growth, development, and reproduction. Metabolic homeostasis depends on endocrine-immune system interactions, yet how lipid droplets and organelles, such as the endoplasmic reticulum, mitochondria, lysosomes, and peroxisomes, contribute to stress-induced lipid dysregulation remains unclear. The present study aimed to synthesize current evidence on redox-mediated regulation of lipid metabolism and lipid metabolic disorders in animals, highlighting recent advances, and identify key directions for future studies. The present study summarized evidence on how different dietary lipid classes influence metabolism and animal health, as well as the role of bioactive nutrients in metabolic programming. The current study described the endocrine functions of the liver, gut, and adipose tissue, as well as the stress-related interactions among these organs. The present study indicated how lipid droplets engaged in dynamic organelle interactions during stress progression and evaluated the potential of lipid-focused nutritional interventions as personalized mitigation strategies. In addition, gut microbiota-derived metabolites and related pathways that contribute to redox imbalance, organelle dysfunction, and stress-associated lipid dysregulation were explored. The current study demonstrated that stress-induced disruptions in lipid metabolism involve intricate, multi-organ, and multi-organelle mechanisms driven by redox changes.

1. Introduction

Lipids comprise a diverse class of biomolecules that support animal physiology as major energy substrates, structural components of cellular membranes, and precursors for signaling mediators[1]. Key lipid classes include triacylglycerols, cholesterol, phospholipids, and non-esterified fatty acids, each contributing to nutrient absorption, energy balance, hormone synthesis, and cellular communication[1]. Disruption of lipid handling can present as dyslipidemia and broader metabolic stress, compromising growth, development, reproductive performance, and immune competence[2]. Metabolic stress related to lipid dysregulation often occurs alongside chronic low-grade inflammation, indicating coordinated endocrine–immune responses. Hormonal regulators such as insulin, glucagon, leptin, and adiponectin regulate lipid storage, mobilization, and utilization, whereas immune mediators released from metabolic tissues, such as adipose tissue and liver, further influence lipid flux and inflammatory reactions[3,4].

Cellular organelles provide the physical and functional platforms that determine lipid fate during health and disease[5]. Lipid droplets store neutral lipids and buffer lipotoxic intermediates by converting excess fatty acids into triacylglycerols and cholesteryl esters[6]. The endoplasmic reticulum (ER) supports lipid synthesis and protein folding,

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and ER stress can promote triglyceride synthesis[7], disrupt proteostasis, and intensify inflammatory signaling[8,9]. Mitochondria generate ATP through fatty-acid β-oxidation and contribute to reactive oxygen species (ROS) production under high substrate flux or respiratory chain strain[10]. Peroxisomes participate in very-long-chain fatty-acid oxidation and generate hydrogen peroxide as a by-product, creating a close link between lipid catabolism and redox balance[11]. Lysosomes play a role in lipid turnover through lipophagy, which is the autophagic process that delivers lipid droplets to lysosomes for breakdown. Impaired lipophagy can lead to longer persistence of lipid droplets and promote ectopic lipid accumulation accumulation[12]. Disrupted communication among organelles can redirect fatty acids toward storage rather than oxidation, increase oxidative injury, and accelerate metabolic dysfunction[13,14]. These alterations emphasized organelle-level mechanisms as essential drivers of stress-linked lipid disorders. Table 1 provides a summary of organelle-specific contributions to lipid metabolism and redox control, illustrating how impairments in lipid droplets, endoplasmic reticulum, mitochondria, lysosomes, and peroxisomes drive lipotoxicity, inflammation, and metabolic disease progression. The present study aimed to synthesize current knowledge on the role of redox signaling in regulating lipid metabolism within animal disorders and to explore its implications for veterinary health.

Table 1. Key cellular organelles in lipid metabolism and redox regulation in pet animals

Organelle	Primary role in lipid metabolism	Role in redox regulation	Interplay with stress/dysregulation	References
Lipid droplets	Store neutral lipids, including triacylglycerols and cholesteryl esters; buffer lipotoxicity by sequestering excess lipids	Accumulate during stress and help protect cells from lipotoxicity	Under stress conditions, lipid droplets undergo dynamic changes in size and number	(6, 7)
Endoplasmic reticulum	Supports lipid synthesis and protein folding	Contributes to reactive oxygen species production during protein folding	Endoplasmic reticulum stress activates the unfolded protein response and alters lipid synthesis and lipid droplet biogenesis	(8, 12, 13)
Lysosomes	Degrade lipids through lipophagy	Participate in the oxidative degradation of cellular components	Lysosomal dysfunction impairs lipid turnover and promotes lipid accumulation	(2, 4, 6, 15)
Mitochondria	Carry out fatty acid oxidation and ATP production	Major site of reactive oxygen species generation through the electron transport chain	Mitochondrial dysfunction increases reactive oxygen species production and contributes to lipotoxicity and metabolic impairment	(3, 6, 16)
Peroxisomes	Perform beta-oxidation of very long-chain fatty acids and synthesize ether lipids	Generate hydrogen peroxide during fatty acid oxidation and contain antioxidant enzymes	Impaired peroxisomal function reduces fatty acid breakdown and increases oxidative stress	(7, 9, 17)

ATP: Adenosine triphosphate

2. Redox signaling and lipid metabolism

Redox signaling represents a core regulatory system in cells and reflects a dynamic balance between the formation and removal of ROS and reactive nitrogen species (RNS)[18]. Although high levels of ROS/RNS can damage biomolecules, controlled ROS/RNS production serves as a signaling mechanism that tunes many cellular functions, including pathways governing lipid metabolism[19]. Major ROS include superoxide anion ($O_2\bullet^-$), hydrogen peroxide (H_2O_2), and hydroxyl radical (•OH), whereas common RNS include nitric oxide (NO•) and peroxynitrite ($ONOO^-$)[20]. Such reactive species are produced during mitochondrial respiration and are generated by enzymes such as nicotinamide adenine dinucleotide phosphate (NADPH) oxidases (NOX), xanthine oxidase, and nitric oxide synthases (NOS). To limit oxidative injury while preserving signaling capacity, cells maintain antioxidant defenses that include enzymatic components (superoxide dismutase, catalase, glutathione peroxidases)[21] and non-enzymatic buffers (glutathione, thioredoxin, vitamins E and C)[22]. Redox status, defined by the balance between ROS/RNS production and antioxidant capacity, shapes the activity of redox-sensitive proteins and signaling pathways that influence lipid handling[23].

Redox regulation affects lipid metabolism at several levels. ROS/RNS can modify the activity of enzymes that control fatty acid synthesis, elongation, desaturation, and oxidation, either directly through oxidative modification or via redox-responsive signaling cascades[24]. For instance, the cellular redox environment can influence key lipogenic enzymes such as acetyl-CoA carboxylase (ACC) and fatty acid synthase (FAS)[25]. Fatty-acid degradation pathways, including mitochondrial and peroxisomal β-oxidation, are sensitive to redox conditions because oxidative stress can impair electron transport, limit ATP production, and alter peroxisomal redox outputs. Redox signaling influences lipid metabolism through transcriptional regulation[26], including modulation of factors such as peroxisome proliferator-activated receptors (PPARs) and sterol regulatory element-binding proteins (SREBPs), which are sensitive to both nutrient status and cellular redox conditions[27]. Sustained redox imbalance that results in oxidative stress is closely linked to lipid metabolic disorders in animals, including obesity, hepatic steatosis, and atherosclerotic changes.

Identifying redox-sensitive control points in lipid metabolism may help guide the development of targeted nutritional and therapeutic approaches for the prevention and management of metabolic diseases[28].

2.1. Dietary lipids in regulating lipid metabolism and animal health

Dietary lipids supply concentrated energy and provide essential fatty acids and fat-soluble vitamins needed for growth, reproduction, immune competence, and cellular membrane integrity[29,30]. After intestinal absorption, dietary fatty acids are transported in lipoproteins to tissues for oxidation, storage, or incorporation into structural and signaling lipids[31]. Dietary fatty-acid profiles can influence tissue fatty-acid composition, membrane fluidity, and inflammatory mediator production, thereby shaping metabolic stability and resilience under stress[32]. Additionally, lipid quality affects redox balance because different fatty acid classes differ in their susceptibility to oxidation and capacity to modulate antioxidant defenses[33].

Fat type plays a major role in oxidative stress and metabolic outcomes[34]. Diets rich in long-chain omega-3 polyunsaturated fatty acids are commonly linked to lower inflammatory signaling and greater redox balance, partly through enhancement of antioxidant defenses and reduction of excessive pro-inflammatory lipid mediators[34-36]. In small-animal practice, omega-3 supplementation is particularly relevant for inflammatory skin and joint disorders, such as canine atopic dermatitis and feline osteoarthritis, where anti-inflammatory lipid mediators and redox modulation may support clinical improvement[37]. By contrast, high intake of saturated fats or oxidized lipids can increase lipid peroxidation and disrupt metabolic function, contributing to dyslipidemia, ectopic lipid accumulation, and tissue dysfunction[38]. A notable clinical example in dogs is the connection between high-fat meals and the risk of pancreatitis, particularly in breeds predisposed to the condition. High-fat diets and hypertriglyceridemia have been linked to pancreatitis in dogs, including Miniature breeds Schnauzers[39]. These findings emphasized that both the amount and quality of dietary fat can directly influence inflammatory damage and oxidative burden in susceptible animals[40].

Furthermore, dietary lipids regulate lipid metabolism through nutrient-sensing pathways that adjust lipid uptake, storage, and oxidation in response to substrate availability[41]. Omega-3–rich profiles tend to promote fatty acid utilization and anti-inflammatory signaling, whereas excess saturated or oxidized fats tend to lead to lipid accumulation and oxidative stress injury[42]. The balance between omega-6 and omega-3 fatty acids is particularly important because both classes compete for enzymatic pathways that generate lipid mediators with opposing inflammatory effects[42]. Practical diet formulation benefits from careful consideration of the total fat level, the distribution of fatty acid classes, the management of freshness and oxidation of fats and oils, and alignment with species- and disorder-specific requirements risk. Such precision is essential for minimizing lipid-driven oxidative stress while preserving essential fatty-acid sufficiency and supporting overall health outcomes[43].

2.2. Natural products in regulating animal lipid metabolism and disorders

Sources of natural nutrients and bioactive compounds have attracted considerable interest for their possible effects on lipid metabolism regulation and the prevention or alleviation of lipid disorders in animals[44]. The most common modes of action of these compounds include anti-oxidant, anti-inflammatory, and direct metabolic regulating effects[45]. Metabolic programming shows that the benefits of early-life nutrition on metabolic health and susceptibility to affective diseases are long-lasting[46]. Polyphenols present in fruits, vegetables, and available in medicinal plants have a high concentration of potent antioxidant and anti-inflammatory effects[47]. A polyphenol compound found in grapes, resveratrol[48], was demonstrated to elevate lipid profiles, decrease oxidative stress, and modulate insulin sensitivity in experimental animals with metabolic syndrome[49]. Its action comprises the activation of sirtuin 1 (SIRT1), a protein deacetylase that is significant in controlling metabolism, and the regulation of lipid biosynthetic and catabolic enzymes[4]. Similarly, the active compound in turmeric, curcumin, has demonstrated hypolipidemic properties and antioxidant activity, thereby improving dyslipidaemia and exerting antioxidant effects in cases of induced obesity in animals[51]. The actions of curcumin can be attributed to the activation of free radical scavenging, the induction of antioxidant enzymes, and the modulation of signaling pathways via PPARs and nuclear factor kappa B (NF-KB)[52].

Another group of natural nutrients with a significant impact on lipid metabolism and redox balance is the omega-3 fatty acids, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA)[53]. Although these acids are classified as dietary lipids, their potential application in cases of lipid disorders warrants discussion separately[54]. It has been reported that omega-3 fatty acid supplementation can decrease triglyceride and lipoprotein levels, as well as inflammation and oxidative stress, in different animals[55]. These beneficial effects of omega-3 fatty acids are due to their ability to inhibit lipogenesis, promote fatty acid oxidation in the kidneys, and regulate the production of pro-inflammatory agents[56]. Additionally, omega-3 fatty acids may affect gene expression, activating PPAR and thereby positively affecting lipid metabolism and antioxidant defence[57]. Important nutrient classes were discussed in Table 2, highlighting their effects on lipid metabolism, redox control, and key mechanistic pathways.

Table 2. Natural nutrients and their roles in lipid metabolism and redox regulation in small animals and wild birds

Nutrient/product class	Examples	Primary effects on lipid metabolism	Effects on redox regulation	Key mechanisms	References
Polyphenols	Resveratrol, curcumin, quercetin	Improve lipid profiles, reduce lipogenesis, and enhance fatty acid oxidation	Act as antioxidants, scavenge free radicals, and increase antioxidant enzyme activity	SIRT1 activation, NF-kB modulation, and PPAR-alpha activation	(51, 52)
Omega-3 PUFAs	Eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA)	Lower triglyceride concentrations suppress lipogenesis and promote fatty acid oxidation	Reduce oxidative stress and modulate eicosanoid production	Modulation of inflammatory signaling pathways	(52, 53)
Vitamins	Vitamin E, vitamin C	Support cellular health and indirectly maintain lipid metabolic function	Protect lipids against peroxidation through antioxidant activity	Direct radical scavenging and regeneration of other antioxidants	(54)
Prebiotics	Inulin, fructooligosaccharides	Modulate gut microbiota, increase short-chain fatty acid production, and reduce inflammation	Indirectly improve redox balance through improved gut health	Selective fermentation by beneficial bacteria and production of SCFAs	(55, 56)
Probiotics	*Lactobacillus* spp., *Bifidobacterium* spp.	Modulate gut microbiota, improve bile acid metabolism, and reduce inflammation	Indirectly supports redox balance through effects on gut health	Competitive exclusion of pathogens, antimicrobial production, and immune modulation	(56, 57)

NF-KB: Nuclear factor kappa B, PPAR: Peroxisome proliferator-activated receptor, PUFAs: Polyunsaturated fatty acids, SCFAs: Short-chain fatty acids, SIRT1: Sirtuin 1

Other non-pharmaceutical products, including prebiotics and probiotics, indirectly affect lipid metabolism by altering the gut microbiota[58]. It is important to note that prebiotics and probiotics influence natural interventions[59]. Prebiotics and probiotic compounds have the potential to enhance nutrient absorption, modulate bile acid metabolism, and reduce systemic inflammation, thereby improving lipid homeostasis and decreasing oxidative stress. Vitamins, including vitamin E and vitamin C, are also important antioxidants that help protect against severe oxidative damage to lipids and support overall metabolic wellness[60,61]. The relative shortage of the following vitamins may intensify oxidative stress and contribute to lipid dysregulation[62]. Numerous natural nutrients and products offer opportunities to address animal lipid disorders through metabolic programming. The variety of actions, frequently involving modulation of redox pathways, raises the possibility of nutritional prevention and correction of metabolic diseases in animals[63].

3. Endocrine roles of liver, gut, and adipose tissue in stress conditions

The liver, gut, and adipose tissue not only process nutrients but also function as endocrine organs, releasing hormones, cytokines, and metabolites that help regulate overall energy balance and lipid metabolism metabolism[64]. Communication among these organs is highly responsive to stress, and stress can disrupt their signaling, increase inflammation, and alter lipid transport and storage[65]. As oxidative burden rises, lipid homeostasis throughout the body becomes increasingly disrupted[66]. The liver plays a central role in controlling lipogenesis, fatty acid oxidation, cholesterol metabolism, and lipoprotein production. However, during chronic inflammation or prolonged nutrient excess, hepatic lipid metabolism can shift toward triglyceride accumulation and steatosis, rendering the liver more susceptible to oxidative injury and metabolic dysfunction[67,68]. Moreover, the liver releases endocrine factors, known as hepatokines, such as fibroblast growth factor 21 (FGF21) and fetuin-A, which can influence insulin sensitivity and lipid use in extrahepatic tissues when stress changes their secretion patterns[69]. The gut contributes to endocrine regulation through hormones including glucagon-like peptide-1 (GLP-1), peptide YY (PYY), and cholecystokinin (CCK), which affect appetite, nutrient handling, and insulin secretion[70]. Stress may weaken gut barrier integrity and increase intestinal permeability, allowing microbial products such as lipopolysaccharide and other luminal signals to enter the circulation[71]. This can further amplify inflammatory signaling in the liver and adipose tissue, worsen redox imbalance, and promote dyslipidemia and hepatic lipid accumulation[72]. Figure 1 shows how stress-driven gut dysbiosis and microbial metabolites influence redox signaling, contribute to liver steatosis and adipose inflammation, and may be counteracted by targeted nutritional strategies[73]. Adipose tissue acts as an active endocrine organ that releases adipokines and inflammatory mediators that influence insulin sensitivity and lipid distribution[74]. Key adipokines include leptin, adiponectin, and resistin, as well as cytokines such as tumor necrosis factor-α (TNF-α) and interleukin-6 (IL-6)[75]. During obesity or chronic inflammatory stress, adipose endocrine output can shift toward a pro-inflammatory profile, contributing to systemic insulin resistance, dyslipidemia, and sustained low-grade inflammation[76]. Communication among the gut, liver, and

adipose tissue occurs through the portal delivery of gut-derived products to the liver and through adipose tissue releasing free fatty acids and adipokines that affect the hepatic metabolism[6]. Stress-activated neuroendocrine signaling, including activation of the hypothalamic-pituitary-adrenal axis and glucocorticoid elevation, can further promote visceral adiposity, hepatic steatosis, and impaired insulin sensitivity, reinforcing endocrine metabolic dysregulation[77].

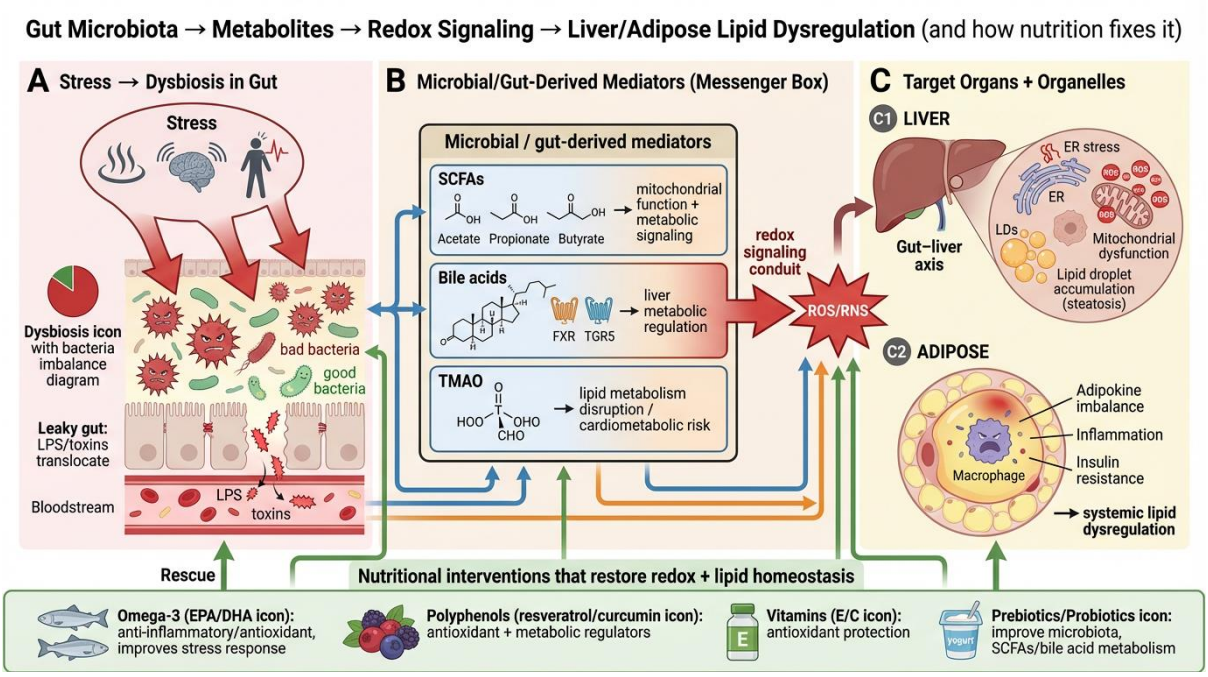

Figure 1. Gut Microbiota, redox, and lipid dysregulation under stress. Under stress, dysbiosis, and increased intestinal permeability allow microbial products and metabolic signals to translocate. These microbial metabolites, including short-chain fatty acids, bile acids, and trimethylamine N-oxide (TMAO), then influence redox signaling and metabolic processes, ultimately affecting hepatic lipid accumulation and adipose inflammation/insulin resistance. Omega-3 fatty acids, polyphenols, vitamins, prebiotics/probiotics can support redox balance and lipid homeostasis. The image was created with PowerPoint and AI (OpenAI, GPT-5.3).

3.1. Response of lipid droplets in stress development

Lipid droplets are dynamic and widespread organelles that function as the main storage sites for neutral lipids, primarily triacylglycerols and cholesteryl esters[78]. Beyond energy storage, lipid droplets contribute to membrane lipid supply, protein sequestration, and signaling. Additionally, lipid droplets provide cytoprotection by buffering excess fatty acids and limiting lipotoxic injury during metabolic stress[79]. Lipid droplet formation is closely associated with the ER. Neutral lipids accumulate between the ER membrane leaflets, then budding occurs to form new lipid droplets in the cytoplasm, which mature by exchanging lipids and proteins with their surrounding organelles[80].

Lipid droplet abundance and composition change rapidly in response to nutrient limitation, ER stress, and oxidative stress[81]. Their formation is often an adaptive mechanism that converts excess free fatty acids into neutral lipids, thereby limiting the buildup of toxic lipid species within the mitochondria and ER. Endoplasmic reticulum stress signaling, including unfolded protein response pathways[82], can further promote lipid droplet formation by increasing triacylglycerol synthesis and stabilizing ER-lipid droplet contact sites that facilitate lipid transfer transfer[83]. Interactions between lipid droplets and mitochondria, lysosomes, and peroxisomes influence cellular stress responses through regulated lipid trafficking. During fasting, lipid droplets can supply fatty acids for β-oxidation, whereas in lipotoxic states, excessive fatty-acid transfer may overwhelm mitochondrial oxidative capacity, increase reactive oxygen species production, and exacerbate cellular injury[84]. Redox state influences lipid droplet dynamics by modulating enzymes involved in triacylglycerol synthesis and lipolysis and by altering organelle contact-site integrity[85]. Oxidative modification of lipid metabolic regulators can alter lipid droplet size and number, while redox-responsive signaling can alter the expression of genes encoding lipid droplet coat proteins and lipid-handling enzymes[86]. Several lipid droplet-associated proteins have mechanistic links between stress signaling and lipid droplet remodeling. These droplets include perilipins (PLIN family), which regulate lipid access at the droplet surface[87]; adipose triglyceride lipase (ATGL/PNPLA2) and hormone-sensitive lipase (HSL/LIPE), which mediate lipolysis, comparative gene identification-58 (CGI-58/ABHD5), serving as an ATGL co-activator, and CIDE family proteins that influence droplet growth and fusion. Under stress conditions, additional functional modules, such as ubiquitin-proteasome components and autophagy-related proteins, are required on the lipid droplet surface. These modules help coordinate

proteostasis and lipid turnover, highlighting a broader role for lipid droplets in cellular adaptation[88].

Feline hepatic lipidosis is a classic example of how adaptive lipid droplet formation becomes problematic and harmful. Anorexia or extended negative energy balance causes rapid breakdown of adipose tissue and increases the delivery of circulating non-esterified fatty acids to the liver[89]. Hepatocellular esterification converts excess fatty acids into triacylglycerols that accumulate as hepatic lipid droplets. Furthermore, the consistent influx may exceed the liver's capacity for oxidation and export, resulting in an overload of lipid droplets[59]. Lipid droplet expansion is linked to mitochondrial stress, increased reactive oxygen species production, lipid peroxidation, and oxidative damage, further impairing liver function and enhancing appetite suppression. This creates a self-perpetuating cycle of anorexia, lipid mobilization, hepatic lipid droplet buildup, and oxidative stress injury[90].

Overall, lipid droplet remodeling acts as a coordinated response to nutrient and redox stress, relying on controlled lipid storage[91], mobilization, and inter-organelle communication. Clarifying how lipid droplets interact with organelles and how their associated proteins are regulated under oxidative stress can aid in developing diagnostic markers and nutritional or therapeutic approaches. These strategies aim to reduce lipotoxicity and maintain organelle function in metabolic disorders[92].

3.2. Nutritional interventions of dietary lipids in response to stress

Dietary lipid planning can lessen stress-associated metabolic dysregulation by reducing lipotoxic exposure, moderating inflammatory signaling[92], and supporting redox homeostasis. Lipid class (omega-3 versus saturated), lipid oxidation status (fresh versus oxidized fats), and total fat load influence mitochondrial ROS production, lipid peroxidation, and control of lipid synthesis and fatty acid oxidation. Practical applications benefit from choosing specific lipids rather than relying on broad high-fat or low-fat diets, particularly in veterinary contexts where dyslipidemia-related disorders are involved common[93].

In small-animal medicine, canine pancreatitis and hypertriglyceridemia-associated pancreatic injury represent clear examples in which dietary lipid control has immediate clinical value[94]. A low-fat, highly digestible diet reduces postprandial triglyceride excursions and limits free fatty acid exposure during lipolysis[95], thereby lowering inflammatory amplification and oxidative burden. Furthermore, fat quality matters[96]. Omega-3 enrichment (EPA/DHA from fish oil or algal sources) can promote a less pro-inflammatory lipid mediator profile and potentially boost antioxidant defenses through redox-sensitive regulatory pathways, as long as the product quality is maintained and oxidation of supplemental oils is minimized[97].

In cats, feline hepatic lipidosis underscores the importance of nutritional strategies that restore positive energy balance and limit persistent hepatic lipid accumulation[98]. Core management emphasizes reliable caloric delivery and high-quality protein to reduce peripheral fat mobilization and support hepatic function. Appetite stimulation and assisted feeding plans are often required to achieve consistent intake[2,99]. Dietary fat should remain moderate rather than extreme, balancing palatability and energy density against the risk of lipotoxicity. Nutrient patterns that promote redox buffering, such as adequate antioxidant micronutrients, can be considered supplementary actions under veterinary supervision, especially when hepatic injury and suspected oxidative stress are present[10]. Conjugated linoleic acid can affect body composition and immune signaling, but results vary by isomer and species, limiting its routine clinical use. Medium-chain triglycerides deliver quickly accessible energy and bypass carnitine-dependent mitochondrial transport. These triglycerides may be useful in specific cases, but caution regarding overall fat sensitivity remains important in dogs with pancreatitis[3]. Overall effectiveness improves when the lipid strategy is combined with complementary measures such as vitamin E and selenium supplementation, microbiome-supportive nutrition (including selected fibers, prebiotics, and probiotics where appropriate), and personalized adjustments based on clinical response and lipid levels[4].

3.3. Effects of gut microbiota on lipid dysregulation under stress or organelle dysfunction

The gut microbiota, a complex community of microorganisms residing in the gastrointestinal tract, plays a profound role in host metabolism, including lipid homeostasis[59]. This microbiome interacts with the host in multiple ways, such as fermenting food components and generating a diverse array of metabolites that can affect host physiology[5]. Recent findings indicate the influential role of stress in the composition and functions of the gut microbiota, which can subsequently contribute to stress-induced lipid disorders and impairments in lipid-metabolic cell organelles function[6].

Exposure to stress, whether environmental, psychological, or physiological, can cause dysbiosis, which is a disturbance of the gut microbial balance community[58]. This dysbiosis may result in changes in the metabolic actions of the microbiota, supporting the production of major metabolites, including short-chain fatty acids (SCFAs), bile acids, and other bioactive molecules[7].

Acetate, propionate, and butyrate are the most common SCFAs produced by dietary fibers and have been demonstrated to play roles in host lipid metabolism as energy providers, in hormone secretion, and in changes in gene expression in metabolic tissues such as the liver and adipose tissue[8]. Stress-related dysbiosis in SCFA production

can mediate the effects of stress-induced dysbiosis on systemic lipid homeostasis.

The bile acids are essential in the digestion and absorption of dietary lipids, which are produced in the liver and metabolized by the gut bacteria[60]. In addition, lipids are signaling molecules that stimulate the nuclear receptors (FXR, farnesoid X) and the G protein-coupled receptor (TGR5) involved in lipid and glucose metabolism, respectively[9]. Changes in gut microbiota due to stress can modulate the deconjugation and transformation of bile acids, and the challenge of changes in the circulating bile acid pool and their resultant effects on host lipid metabolism and intracellular signaling pathways[71]. Moreover, intestinal microbiota can produce another substance, trimethylamine n-oxide (TMAO), which has been linked to cardiovascular disease and disrupted lipid metabolism in certain reports[11]. The gut microbiota or its metabolites may directly or indirectly affect the function of several cell organelles involved in lipid metabolism, such as lipid droplets, ER, mitochondria, lysosomes, and peroxisomes[63]. For instance, SCFAs have the potential to influence mitochondrial activity and tissue organogenesis [10]. Gut microbiota-derived products have the potential to influence ER stress and the unfolded protein response, which are closely linked to lipid metabolism and LD formation[10]. This is especially significant to the gut-liver axis, which is a two-way communication between the gut and the liver[11]. The gut microbiota and the products delivered to the liver through the portal vein directly influence hepatic lipid metabolism and contribute to the development of fatty liver disease stress[12]. The redox signal is a vital pathway for communication between the gut microbiota, host tissues, and organelles[70]. Dysbiosis may cause both microbiota and the host immune system in the gut to produce more ROS or RNS, therefore contributing to intestinal oxidative stress. Locally developed oxidative stress can have systemic effects, reflected in the redox status of remote organs involved in lipid metabolism[13]. In addition, gastrointestinal tract microbiota-derived metabolites can directly regulate host antioxidant defense mechanisms and redox-sensitive signaling pathways, and affect lipid homeostasis and organelle activity[99]. Some SCFAs demonstrated antioxidant properties and activated the predicted Nrf2 pathway, a key regulator of antioxidant gene expression[14]. The complex interplay between stress and gut microbiota, each with metabolites, redox signaling, and organelle activity, is essential for understanding how stress can be intervened upon in animals to improve lipid dysregulation[6].

4. Clinical relevance of lipid dysregulation in companion animals

Lifestyle-associated metabolic disease in dogs and cats is increasingly characterized by excess adiposity, dyslipidemia, and chronic low-grade inflammation, with oxidative stress acting as a reinforcing factor for lipid imbalance[68]. Redox imbalance can increase lipotoxic injury through organelle-level mechanisms, such as mitochondrial ROS production during fatty acid oxidation, endoplasmic reticulum stress responses that promote lipid synthesis and impair protein folding, and maladaptive lipid droplet remodeling that facilitates ectopic lipid accumulation deposition. Common clinical patterns in small-animal practice, including obesity, diabetes phenotypes, hypertriglyceridemia-related pancreatitis risk (especially in dogs), and hepatic lipid disorders (notably feline hepatic lipidosis), all involve mechanisms such as lipid overload, inflammatory responses, and compromised redox balance capacity[16].

Translational management aligns with reducing lipid oversupply and restoring metabolic flexibility[2]. Nutritional strategies include controlled energy intake for weight loss, syndrome-specific macronutrient modifications, and careful management of dietary fat in individuals with hyperlipidemia or pancreatitis dogs[89]. In cats exhibiting insulin-resistance phenotypes, a diet that promotes glycemic stability along with gradual weight loss can help decrease the glucolipotoxic stress on the liver and pancreas. Diet quality is also important, including minimizing oxidized fats and emphasizing lipid sources linked to lower inflammatory signaling, which can support redox balance stability. Adjunctive supplementation offers specific redox support instead of substituting dietary correction. This adjunctive supplementation includes antioxidant nutrients and mitochondrial support, supervised by a veterinarian and tailored to species-specific safety guidelines. Clinical monitoring using body condition scoring, serum triglycerides and cholesterol fractions, and liver-associated enzymes is needed for a greater diet[18].

5. Lipid dysregulation in wild birds

Wild birds in rehabilitation, captivity, or urban areas can develop lipid metabolic issues due to high-energy diets, reduced activity, and chronic stress[24,63,66]. Obesity, hepatic lipid accumulation, and vascular lipid lesions reported in avian practice are often caused by an imbalance between dietary energy intake and species-appropriate metabolism demand[19]. Redox imbalance can contribute to avian lipid pathology by inducing oxidative injury in hepatic tissue, mitochondrial dysfunction during high lipid flux, and inflammatory amplification driven by stress hormones and environmental challenges[6,20,41]. Such mechanisms align with a redox organelle framework in which sustained oxidative stress disrupts lipid handling and accelerates tissue injury[20].

In avian contexts, practical translation mainly focuses on prevention and providing supportive care through proper nutrition husbandry[27,35,72]. Shifting the diet from energy-dense, seed-heavy patterns to species-appropriate nutrient profiles, combined with foraging enrichment and activity promotion, can reduce lipid overload and improve metabolic health resilience[24,27,33]. Stress reduction through environmental optimization and minimizing repeated

handling can further limit oxidative burden[21,42]. In rehabilitation settings, gradual improvement in body condition, careful control of lipid intake during recovery, and regular monitoring of liver function indicators help ensure a safer transition of metabolic processes[22,48,66]. Nutritional antioxidant support can be considered an adjunct when oxidative injury is suspected, but the focus remains on addressing the primary factors, including diet composition, activity opportunities, and chronic stress exposure, given the strong connection between lifestyle factors and redox-related lipid dysregulation[22,24].

6. Conclusion

The present study indicated that redox regulation plays a central role in the pathogenesis of lipid metabolic disorders in animals. The current evidence reflected a complex interplay among cellular pathways, organs, and gut microbiota. These interactions are important to understanding conditions such as obesity, pancreatitis in dogs, fatty liver disease in cats, and similar health issues found in urban wild birds. While the present study supported targeted nutritional and management strategies to mitigate oxidative stress and lipotoxicity, future studies should focus on species-specific biomarkers, controlled dietary intervention trials, and further exploration of organelle interactions and microbiome-derived metabolites to improve diagnosis, treatment, and prevention of diseases, especially in animals.

Declarations

Ethical considerations

Ethical issues, including plagiarism, consent to publish, misconduct, data fabrication and falsification, double publication, submission and redundancy, have been checked by all authors. No AI tool was used to generate scientific content, interpret data, draw conclusions, or create references. The figure was designed by the authors using ChatGPT (OpenAI, GPT-5.3), and the authors take full responsibility for using AI tools for generating the image in the present study.

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Authors' contributions

Umar Aziz and Muhammad Hanzalah Yousaf conceived and designed the review. Umar Aziz, Abdul Rehman, Muhammad Waqar, and Nimra Safdar Ali performed the literature search and compiled the relevant studies. Umar Aziz drafted the manuscript, and Umar Aziz, Muhammad Waqar, Nauman Khan, and Muhammad Hanzalah Yousaf prepared the figures and visual content. Abdul Rehman, Nimra Safdar Ali, and Muhammad Mushahid critically revised the manuscript for important intellectual content. All authors contributed to writing and editing the review, read and approved the final edition of the manuscript.

Availability of data and materials

No new data were generated in support of the present review. All information is contained within the published literature cited in this article.

Competing interests

The authors declare that they have no competing interests.

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