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Review Article

Ferroptosis in Autoimmune Disorders, Viral, and Bacterial Infections

Alireza Zafarani M.Sc., Ali Amini * Ph.D.

Department of Hematology and Blood Banking, Faculty of Allied Medicine, Iran University of Medical Sciences, Tehran, Iran

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A B S T R A C T

Ferroptosis is a type of cell death associated with excess intracellular iron and lipid peroxidation, distinct from other types of cell deaths by function and morphology. The role of ferroptosis in autoimmune disorders, which are related to inadequate removal of dead cells and debris, and infectious disorders like bacterial and viral infection have been discussed vastly. Overall, this review provides a comprehensive update on the role of ferroptosis in autoimmune and infectious diseases and suggests that targeting ferroptosis may have therapeutic potential for treating these diseases.

***Corresponding Author:** Department of Hematology and Blood Banking, Faculty of Allied Medicine, Iran University of Medical Sciences, Hemmat Highway, Tehran, Iran. **Postcode:** 1449614535, **Tel:** +982186704665, **Fax:** +982188622576, **Email:** amini.a20@iums.ac.ir

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Introduction

Infectious and autoimmune diseases are two of the most severe health issues that continue to affect millions of individuals worldwide. While antibiotics or immune system suppression are frequently used to treat these disorders, recent research has discovered a unique and potentially successful therapeutic alternative called ferroptosis [1, 2]. Iron-dependent lipid peroxidation is a hallmark of ferroptosis, a recently discovered regulated cell death. A web of molecular pathways carefully controls this process, essential for managing cellular homeostasis. Researchers have found connections between ferroptosis dysregulation and several clinical diseases, including autoimmune disorders and infectious diseases [3]. A chronic inflammatory response and tissue damage result from autoimmune diseases when the immune system attacks host cells wrongly. Ferroptosis, which controls how immune cells behave, has been associated with the initiation and development of autoimmune illnesses such as rheumatoid arthritis (RA), lupus, and multiple sclerosis (MS) [1]. Bacteria and viruses can alter cellular processes in infectious diseases to help survival and replication. It has been shown that ferroptosis helps the host's defense against infection. Deregulation of this mechanism has been connected to developing viral illnesses such as hepatitis C and the human immunodeficiency virus (HIV). By concentrating on the molecular processes that govern ferroptosis and finding a technique to block ferroptosis in autoimmune illnesses to prevent normal cells from being damaged, researchers may be able to develop innovative drugs that enhance the body's natural immune response to these infections [2]. This article will discuss the role of ferroptosis in autoimmune disorders and infectious diseases. The review explores the latest research on the molecular mechanisms regulating ferroptosis. It discusses the potential implications of targeting these pathways for developing new therapies. We will also highlight the challenges and opportunities in translating these findings into clinical applications to improve patients' lives with autoimmune disorders and infectious diseases.

Ferroptosis

Ferroptosis is a unique, newly discovered form of regulated cell death known by the accumulation of high levels of lipid peroxides due to iron metabolism dysregulation. Unlike other forms of cell death, such as apoptosis, necroptosis, and pyroptosis, ferroptosis does not involve death receptors or sensors to trigger the process. Instead, small molecules can induce it by inhibiting the activity of system Xc^-, a cystine/ glutamate antiporter essential for glutathione synthesis. Ferroptosis can also be triggered by various stressors such as oxidative stress, endoplasmic reticulum stress, and mitochondrial dysfunction. Due to its unique features, ferroptosis is implicated in various pathologic conditions, including cancer, autoimmunity, infections, neurodegeneration, and ischemic tissue injury [4] (Fig. 1). Morphologically, ferroptosis is characterized by intact but lucent mitochondria, normal nuclear size and chromatin., and the absence of significant plasma membrane rupture or blebbing.

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Biochemically, ferroptosis involves intracellular glutathione depletion and decreased glutathione peroxidase 4 (GPX4) activity, which leads to lipid peroxides and reactive oxygen species (ROS) accumulation that promotes ferroptosis. Genetically, ferroptosis is a biological process regulated by multiple genes that involve changes in iron homeostasis and lipid peroxidation metabolism [5].

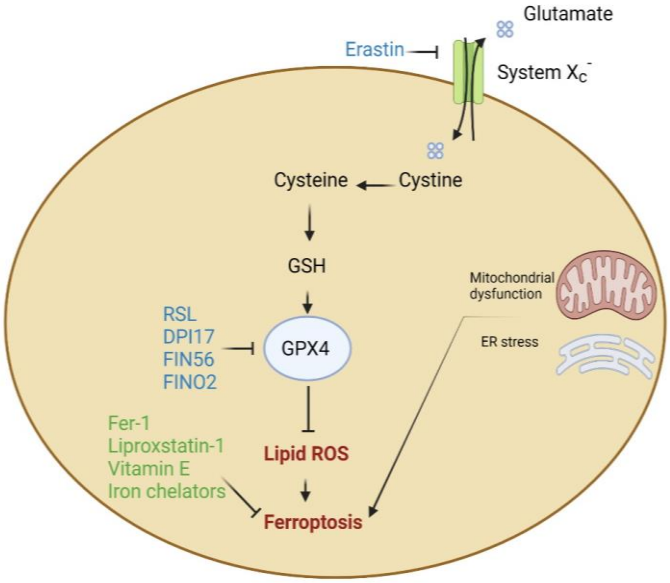

Fig. 1. Ferroptosis formation, its activator, and inhibitor. System X_c^- enters cystine and exits glutamate; this process elevates cysteine in the cell, which finally leads to the production of glutathione and glutathione peroxidase 4. Glutathione peroxidase 4, an enzyme, inhibits lipid peroxides, reactive oxygen species formation, and ferroptosis.

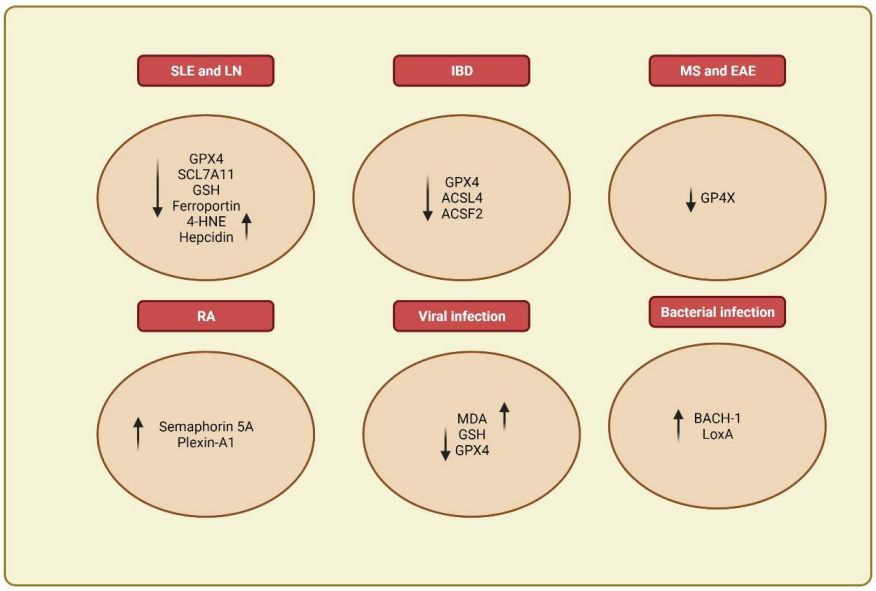

Fig. 2. Decrease or increase of ferroptosis-related compounds in different diseases.
SLC7A11= Solute Carrier Family 7 Member 11; 4-HNE= 4-Hydroxynonenal; ACSL4= Long-chain acyl-CoA synthase-4; ACSF2= Acyl CoA synthetase family member 2; MDA= Malondialdehyde; BACH-1= BTB Domain And CNC Homolog 1; LoxA= Lipoxygenase A; SLE; Systemic lupus erythematosus; LN= Lupus nephritis; IBD= Inflammatory bowel disease; MS= Multiple sclerosis; EAE= Autoimmune encephalomyelitis; RA= Rheumatoid arthritis.

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Table 1. The ferroptosis inhibitor drugs used in autoimmune diseases and their effects

Disease name	Drug	Mechanism	Effect
SLE	Liproxstatin-1	Activating GPX4 [10, 11]	Neutrophils from healthy control cocultured with SLE serum, and Liproxstatin-1 show improved cell viability.
Lupus nephritis	Liproxstatin-2	Inhibit lipid peroxidation [13]	Reduced human proximal tubular cells susceptibility to ferroptosis by Liproxstatin-2.
Ulcerative colitis	Shaoyao Decoction	Activating GPX4 [30]	SYD significantly reduced ferroptosis in epithelial cells of rats with colitis
	Fer-1	Regulation of ACSF2 expression [31]	NA
	Deferasirox	Regulation of iron storage [32]	Deferasirox provided substantial relief for mice's ulcerative colitis induced by DSS. This was observed through improvements in various parameters, including weight loss, survival rate, reduction in colon length, DAI score, and histology score.
Multiple sclerosis	Lapatinib, Ferrostatin and Liproxstatin-1	Activating GPX4 [34]	NA
Rheumatoid arthritis	Semaphorin 5A	enhanced GPX4 expression [36]	Semaphorin 5A triggers the activation of the PI3K/AKT/mTOR signaling pathway, which leads to an increase in the expression of GPX4 and the activation of SREBP1/SCD-1 signaling. As a result, the process of ferroptosis in rheumatoid arthritis synovial fibroblasts is suppressed in the cells taken from the patients.
Tuberculosis	Ferrostatin-1	Activating GPX4 [51]	The process of ferroptosis in cultures of macrophages infected with Mycobacterium tuberculosis was prevented when treated with Fer-1

GPX4= Glutathione peroxidase 4; SLE= Systemic lupus erythematosus; SYD = Shaoyao decoction; ACSF2= Acyl CoA synthetase family member 2; DSS= Dextran sulfate sodium; DAI= Disease activity index

Erastin and RAS synthetic lethal 3 (RSL3) are classical ferroptosis activators that hinder the antioxidant system and promote iron buildup within cells. This excess iron can produce harmful ROS through the Fenton reaction, causing oxidative damage. Furthermore, iron can enhance the activity of enzymes like lipoxygenase (ALOX) and prolyl hydroxylases, which play roles in lipid peroxidation and oxygen regulation.

Lipid peroxidation, primarily affecting unsaturated fatty acids in cell membranes, is a crucial process in ferroptosis. Specific genes/ proteins like Long-chain acyl-CoA synthase-4 (ACSL4) are known to be overexpressed and serve as biomarkers and drivers of ferroptosis. Ferroptosis can result in the demise of specific types of immune cells, leading to a loss of immune function.

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Conversely, it can trigger inflammation and contribute to tissue damage, thereby contributing to the progression of different diseases. Hence, inhibiting ferroptotic cell death can be achieved by targeting genes associated with iron overload or using iron-chelating agents. Additionally, activating genes involved in antioxidant defense and membrane repair can mitigate membrane damage caused by ferroptosis. The outcome of cells exposed to ferroptotic stimuli is determined by the balance between detrimental and protective responses, determining whether the cells survive or perish [6].

Various substances fall into four categories that can induce ferroptosis: Erastin, RSL3, DPI7, FIN56, and FINO2. Erastin was the first compound with selectively lethal effects on RAS-expressing cancer cells found to cause ferroptosis. Erastin inhibits system Xc^-, reducing glutathione levels and mitochondrial dysfunction. RSL3 and DPI7 directly inhibit GPX4 activity, while FIN56 promotes GPX4 degradation and depletion of the endogenous antioxidant coenzyme Q10 (COQ10). FINO2 causes ferroptosis by directly oxidizing labile iron and inactivating GPX4 [7]. Many specific inhibitors of ferroptosis, such as Fer-1, liproxstatin-1, vitamin E, and iron chelators, have been identified, which inhibit the formation of lipid peroxides and protect against ferroptosis.

Autoimmune disorder and ferroptosis

Autoimmune diseases are complex, and their exact causes are not fully understood. Although they may share some clinical similarities, each autoimmune disease has unique characteristics. For example, RA typically affects hand joints with less involvement of major organs, while systemic lupus erythematosus (SLE) can affect multiple organs due to autoantibody production and immune complex deposition. Inflammatory bowel disease (IBD) may also present with joint inflammation, but its primary manifestation is chronic intestinal inflammation. Researchers have explored various factors contributing to immune activation in autoimmune diseases, abnormal or increased cell death, and impaired removal of dead cells, which can release intracellular contents and trigger inflammation [8, 9].

Ferroptosis in systemic lupus erythematosus and lupus nephritis

SLE is an autoimmune disorder characterized by the excessive production of autoantibodies that target cellular components within the nucleus, cytoplasm, and cell membrane. This immune response leads to the formation and deposition of immune complexes in tissues and organs, leading to organ damage. Cell death amplifies the immune response, exposing intracellular contents to the immune system. Consequently, the clearance or uptake of dead cells by macrophages can be compromised, resulting in immune reactions. Recent research has unveiled the crucial role of ferroptosis in developing SLE [8].

SLE patients show reduced expression of GPX4 in neutrophils, which prevents lipid peroxidation and maintains membrane integrity [10, 11]. Studies have shown that the downregulation of GPX4 expression induced by interferon-α (IFN-α) leads to neutrophil ferroptosis in SLE patients. The activated Ca^{+2}/

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calmodulin-dependent kinase IV (CaMKIV)/ cAMP-responsive element modulator α (CREMα) axis in T lymphocytes of SLE patients regulates GPX4 expression. Furthermore, the genetic knockdown of CREMα led to the recovery of GPX4 expression levels in SLE neutrophils [10, 12]. Mice with a specific deficiency of GPX4 in myeloid cells exhibited several hallmark features associated with lupus, including the production of antibodies targeting double-stranded DNA (anti-dsDNA antibodies), skin lesions' development, and proteinuria. Disease severity could be significantly reduced by treatment with a specific ferroptosis inhibitor. These findings suggest that regulating ferroptosis is essential for preventing SLE pathogenesis [10]. Patients with lupus nephritis and mice models of the disease exhibited increased lipid peroxidation in the tubular segments of their kidneys, along with elevated Acyl-CoA synthetase long-chain family member 4, an enzyme that promotes ferroptosis. Additionally, the nephritic mice showed reduced expression of Solute Carrier Family 7 Member 11 (SLC7A11), a cystine importer, impaired glutathione synthesis, and decreased levels of GPX4. Lipidomics analysis confirmed the occurrence of ferroptosis in the kidneys of these mice. In mice with immune complex glomerulonephritis induced by nephrotoxic serum, impaired iron sequestration in the proximal tubules exacerbated ferroptosis. The serum obtained from lupus nephritis patients rendered human proximal tubular cells more susceptible to ferroptosis, which could be inhibited by Liproxstatin-2, a novel ferroptosis inhibitor [13]. The study discovered a notable increase in the expression of 4-Hydroxynonenal (4-HNE), a marker associated with ferroptosis activation, in both the glomeruli and tubulointerstitium of individuals with lupus nephritis. Transcriptomic analysis revealed significant alterations in genes related to iron metabolism, antioxidant system inhibitors, and ferroptosis suppressors in lupus nephritis. Among these genes, *LTF*, *CYBB*, and *CCL5* were found to be upregulated, while *G0S2* and *AKR1C1* were downregulated in both the glomeruli and tubulointerstitium of lupus nephritis patients. These findings suggest these genes could be potential biomarkers for ferroptosis in lupus nephritis [14].

Iron dysregulation is strongly associated with ferroptosis, and studies have indicated a strong relation between iron level and SLE [15]. Ferroportin is the sole exporter responsible for releasing ferrous iron from the cytoplasm. The regulation of ferroportin expression is intricate and varies across different cell types. Its membrane-associated levels are controlled by its ligand, hepcidin, a peptide produced by the liver and regulated by iron levels. When hepcidin binds to ferroportin, it internalizes ferroportin and its subsequent degradation in lysosomes, thereby reducing iron availability. Interleukin(IL)-6, a pro-inflammatory cytokine elevated in SLE patients, can modulate hepcidin expression and promote iron retention by downregulating ferroportin in macrophages (15-17). In addition, the accumulation of immune complexes in the glomerulus of the kidney triggers

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inflammatory reactions and increases hepcidin expression. Studies have shown that patients with SLE have reduced iron availability compared to healthy controls due to a decrease in the level of transferrin. The serum transferrin concentration is inversely related to disease status in patients with SLE [18-20] (Fig. 2 & Table 1).

Ferroptosis in IBD

Chronic inflammation of the intestinal epithelium is a hallmark of IBD, such as Crohn's disease (CD) and ulcerative colitis (UC) [21]. This chronic inflammation often leads to increased cell death within the intestine and colon, making it essential to carefully regulate cell regeneration and cell death processes. Studies have identified several cell death subtypes that contribute to the development of chronic intestinal inflammation [21].

Iron plays a vital role in regulating cell death and tissue regeneration processes. Excessive iron supplementation can result in iron deposition in the intestine, increasing ROS production and causing intestinal inflammation in animal models of IBD. The effects of iron supplementation on the gut microbiota can be beneficial or detrimental, depending on the dosage and duration of exposure [22-24].

Polyunsaturated fatty acids (PUFAs) like arachidonic acid and linoleic acid are highly prone to oxidation by ROS. The buildup of ROS, both in the cytosol and within lipids, serves as a strong stimulus for the oxidation of PUFAs, leading to the formation of lipid peroxides and ultimately triggering ferroptosis. In mice, consuming a Western diet rich in PUFAs induces lipid peroxidation and inflammation in the intestines, producing symptoms reminiscent of characteristics observed in small intestinal CD [25-27].

Notably, ferric iron enhances lipid peroxidation and the production of cytokines induced by arachidonic acid in intestinal epithelial cells (IECs) with reduced levels and activity of GPX4, an enzyme that protects against lipid peroxidation. The enzyme ACSL4, responsible for attaching long PUFAs to coenzyme A, promotes the esterification of arachidonic acid into phospholipids, facilitating the peroxidation process. In contrast, IECs derived from the affected mucosa of small intestines in patients with CD exhibit decreased levels of GPX4 and lipid peroxidation [27, 29]. In a study, Shaoyao Decoction (SYD), a canonical herbal, reduced chemical-induced colitis by activating GPX4, inhibiting ferroptosis in epithelial cells, and restoring barrier function. The therapeutic effects of SYD were attributed to the presence of certain compounds such as wogonoside, wogonin, palmatine, paeoniflorin, and liquidity [30]. The acyl CoA synthetase family member 2 (ACSF2) was reduced in animals with UC and *Salmonella typhimurium* colitis and cell models.

Additionally, in cell models induced with Lipopolysaccharide, the inhibitor Fer-1 reversed the expression of *ACSF2*, suggesting that *ACSF2*, a gene related to ferroptosis, plays a crucial role in regulating inflammation and ferroptosis. This finding suggests that *ACSF2* could be a potential target for future research [31]. In mice with UC, ferroptosis was

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triggered, as shown by an accumulation of ferrous iron, increased production of ROS, depletion of essential antioxidants, and decreased expression of specific genes *GPX4*. However, these changes were strongly reversed when the mice were treated with deferasirox. Notably, deferasirox treatment also impacted the composition of the intestinal microbiota [32] (Fig. 2 & Table 1).

Ferroptosis in MS and autoimmune encephalomyelitis

MS is a long-lasting inflammatory disorder affecting the human's central nervous system. The disease is characterized by inflammation around blood vessels, loss of myelin (demyelination), death of oligodendrocytes, and degeneration of nerve cells. A study found that GPX4 mRNA and protein levels are reduced in the gray matter and spinal cord tissues of MS and autoimmune encephalomyelitis. The decrease in GPX4 and other enzymes that help maintain normal levels of glutathione led to the accumulation of lipid peroxidation compounds and changes in the lipid composition. This and abnormal mitochondrial morphology suggest that ferroptosis damage occurs in these demyelinating inflammatory disorders [33]. Research aimed to find potential drugs for MS by targeting the GPX4 protein using a computational approach reported some anti-cancer drugs as a potential option for treating MS by activating GPX4. Previous studies have shown that Lapatinib, a kinase inhibitor, can activate GPX4 and prevent neuronal death caused by ferroptosis, which is linked to MS and other neurodegenerative diseases. Ferrostatin and Liproxstatin-1 can also restore GPX4 activity by inhibiting oxidative stress [34] (Fig. 2 & Table 1).

Ferroptosis and RA

RA is a chronic inflammatory disorder that leads to synovial inflammation, proliferation, and joint destruction. Oxidative stress plays a significant role in RA's pathogenesis by increasing ROS production and inducing synovial fibroblast proliferation and synovitis. In particular, lipid peroxidation and ferroptosis are believed to be critical for synovial fibroblast proliferation and survival in the inflamed joints of RA patients [8, 35].

Research has revealed that suppressing ferroptosis in synovial fibroblasts is a mechanism to sustain the inflammatory state in joints. For example, the administration of imidazole ketone erastin (IKE), a compound that induces lipid peroxidation and ferroptosis, decreases the severity of synovitis. In mice with collagen-induced arthritis (CIA), this treatment prevents the development of arthritis and protects against joint damage. The GPX4 inhibitor RSL3 explicitly promotes cell death in fibroblast activation protein-α (FAPα)+ fibroblasts. These fibroblasts are usually absent under non-inflammatory conditions but significantly increase the inflamed synovium of mice with CIA (35).

Additionally, it has been observed that TNF protects ferroptosis in human synovial fibroblasts exposed to ferroptosis-inducing substances like IKE and RSL3. Treatment with IKE resulted in the depletion of glutathione, a cellular antioxidant, while TNF administration reversed this effect and increased glutathione

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levels in synovial fibroblasts. TNF treatment did not impact iron availability but enhanced the expression of various regulators associated with glutathione biosynthesis. These findings suggest that the therapeutic benefits of anti-TNF biologics in RA patients may partly be attributed to the blocking of TNF-mediated protection of synovial fibroblasts in inflamed joints [35]. The researchers found that Semaphorin 5A levels, related to different pathological processes such as the movement of cells, the development of tumors, and the response of the immune system were higher in RA patients than in osteoarthritis patients, and its elevation promoted cytokine secretion, proliferation, and migration while reducing apoptosis of synovial fibroblasts. This effect was mediated through increased binding between Semaphorin 5A and its receptors, mainly derived from $CD68^+$ synovial macrophages. The study also showed that Plexin-A1 expression was elevated in RA synovial fibroblasts and that knockdown of both Plexin-A1 and Plexin-B3 abolished the effect of Semaphorin 5A on SF activation. Furthermore, Semaphorin 5A was found to activate the PI3K/AKT/mTOR signaling pathway and inhibit ferroptosis, which was confirmed by transcriptome sequencing and protein array detection. The study also demonstrated that Semaphorin 5A enhanced GPX4 expression and SREBP1/SCD-1 signaling to suppress RA synovial fibroblasts' ferroptosis, which suggests Semaphorin 5A inhibitor as an excellent option for the treatment of patients with RA [36] (Fig. 2 & Table 1).

Ferroptosis in viral infections

Viral infections can influence lipid peroxidation levels in infected cells, resulting in elevated levels of lipid peroxidation products in the bloodstream. In the case of chronic hepatitis C infection, patients often display increased serum levels of lipid peroxidation products like Malondialdehyde, which are induced by the production of ROS triggered by the Hepatitis C virus (HCV). This oxidative stress caused by lipid peroxidation has been demonstrated to contribute to the progression of hepatitis infection and liver damage [37]. The regulation of cellular lipid metabolism, which plays a role in restricting HCV replication, remains poorly understood. Recent studies indicate that the mechanism behind HCV restriction resembles the iron-dependent pathway that triggers ferroptosis. Fatty Acid Desaturase 2 (FADS2), an enzyme responsible for converting oleate into Mead acid and other highly unsaturated fatty acids, plays a crucial role in this process. Genetic depletion and ectopic expression experiments have demonstrated that FADS2 is essential for determining cellular sensitivity to ferroptosis; inhibiting FADS2 significantly increases HCV replication. Additionally, the ferroptosis-inducing compound erastin modifies the conformation of the HCV replicase, rendering it more susceptible to antiviral agents targeting the viral protease. These findings highlight the significance of FADS2 as a critical factor in ferroptosis regulation and suggest that manipulating the ferroptosis pathway could be a potential strategy to reduce viral replication [38]. Similarly, human immunodeficiency

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virus (HIV) is associated with oxidative stress, reduced glutathione levels, and increased Malondialdehyde concentration in serum, which can stimulate viral replication and favor disease progression [39]. N-acetylcysteine (NAC) is a compound that supplies cysteine, an essential component for the production of glutathione. Research has demonstrated that NAC can inhibit the replication of HIV in infected T cells, chronically infected monocytic cells, and peripheral blood mononuclear cells infected in laboratory settings. Additionally, both glutathione and glutathione esters can impede the transcription of HIV stimulated by cytokines. Low levels of glutathione have been linked to decreased survival rates in HIV-infected patients, and antioxidant substances have been proposed as potential adjunctive therapy for HIV infection [39, 40].

T cells with reduced levels of glutathione demonstrate a diminished ability to generate Interferon-gamma and IL-12 cytokines, which promotes the proliferation of *M. tuberculosis* within infected myeloid cells. Preclinical investigations on HIV-associated patients have revealed that liposome-encapsulated NAC leads to enhanced cytokine production, indicating a positive effect [41, 42]. Restoring glutathione levels with NAC supplementation enhances cytokine production by T cells and promotes the ability of macrophages to clear *M. tuberculosis* in cells co-infected with HIV and Mtb. Encouraging results from randomized phase II clinical trials have demonstrated that NAC treatment improves the redox status of HIV-associated tuberculosis patients and reduces the production of lipid peroxide products like Malondialdehyde [41-44]. During viral infections, including Coronavirus Disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), RNA viruses have been observed to produce ROS. The excessive release of cytokines, known as a cytokine storm, often seen in COVID-19 patients, along with elevated levels of ferritin, could contribute to ROS generation through the Fenton reaction. Furthermore, SARS-CoV-2 infection has been found to downregulate the expression of several genes encoding antiferroptotic enzymes, including GPX4 protein [45-48]. Hence, it is possible to hypothesize that infection with SARS-CoV-2 could result in elevated iron levels, the generation of ROS, and lipid peroxidation, consequently initiating ferroptosis and contributing to different pathological conditions associated with COVID-19. These conditions may include the cytokine storm and the development of multiorgan failure (Fig. 2).

Ferroptosis in bacterial infection

Recent research has provided insights into the involvement of ferroptosis in infectious diseases, specifically tuberculosis and Pseudomonas aeruginosa infections. In the case of tuberculosis caused by *Mycobacterium tuberculosis*, it has been discovered that *Mycobacterium tuberculosis* can induce pathological ferroptosis in macrophages. This process can be counteracted by administering ferrostatin-1, a lipophilic antioxidant, and iron chelators, which safeguard the lungs against

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Mycobacterium tuberculosis-induced damage and aid in eradicating the pathogen. Additionally, the transcription factor BTB Domain And CNC Homolog 1 (BACH-1) has been identified as an inhibitor of *GPX4* expression in macrophages, thereby promoting ferroptosis in response to *Mycobacterium tuberculosis* infection [49-53] (Table 1).

In the context of *Pseudomonas aeruginosa* infections, the bacteria release a virulence factor known as lipoxygenase A, which induces phospholipid peroxidation in the airways of individuals with cystic fibrosis or those affected by nosocomial infections. This process sensitizes bronchial epithelial cells to ferroptosis upon infection with *Pseudomonas aeruginosa*. Another enzyme produced by *Pseudomonas aeruginosa*, called elastase, can cleave transferrin-bound iron, facilitating iron uptake by the bacteria and leading to the production of peroxidized phospholipids in neighboring cells through the Haber-Weiss reaction. The potential involvement of ferroptosis in various infectious scenarios resulting from these mechanisms is yet to be fully elucidated [54] (Fig. 2).

Conclusion

This review discussed ferroptosis, its inhibitor, and its activators. The role of ferroptosis in autoimmune disorders and bacterial and viral infections has been discussed. We showed how ferroptosis is dysregulated in mentioned diseases and certain inhibitor and activator works in favor of diseases. Several treatment options have been reviewed. Generally, ferroptosis is a new area with many undiscovered that need to be discussed further.

Conflict of Interest

The authors declare that the research was conducted without any commercial or financial relationships construed as a potential conflict of interest.

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