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Inflammatory Pathways: A Review of the Complex Interaction between Infection, Chronic Diseases and Psychiatric Disorders

Taiwo S Agidigbi [a*], Grace P Adeniyi [b], Bolanle A Adeniyi [c], Oluyinka E Majekodunmi [b] and Gail B Mahady [d]

[a] Department of Orthopedics and Rehabilitation, Yale School of Medicine, New Haven, CT, USA.
[b] Federal Neuropsychiatry Hospital Aro, Abeokuta, Ogun State, Nigeria.
[c] Department of Pharmaceutical Microbiology, University of Ibadan, Nigeria.
[d] Department of Pharmacy Practice, University of Illinois, Chicago, IL, USA.

Authors' contributions

This work was carried out in collaboration among all authors. Authors TSA, GPA and BAA designed the study, drafted the outlines, and wrote the first draft of the manuscript. Authors TSA, GPA, BAA, OEM and GBM managed the literature search. All authors read and approved the final manuscript.

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ABSTRACT

Inflammation plays a pivotal role in both acute and chronic diseases, acting as a central mediator between infection and various non-communicable diseases. Recent research has highlighted the intricate interplay between inflammatory pathways, chronic conditions such as cardiovascular disease, diabetes, neurodegenerative disorders, and psychiatric conditions like depression and

**Corresponding author: E-mail: samuelgeneration015@gmail.com, taiwo.agidigbi@yale.edu;*

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anxiety. This review explores the molecular mechanisms by which inflammation influences these complex interactions, emphasizing the role of cytokines, immune responses, and cellular stress. We critically analyze current literature on how infections, including viral and bacterial pathogens, can trigger or exacerbate systemic inflammation, contributing to the progression of chronic illnesses and psychiatric disorders. Additionally, we investigate how chronic diseases, and psychiatric conditions may reciprocally affect immune regulation, fostering a vicious cycle of inflammation. Understanding these relationships provides insights into novel therapeutic targets such as application of probiotics and natural products aimed at modulating inflammatory responses to improve outcomes in both physical and mental health.

Keywords: Inflammatory-pathways; infection; chronic-disease; psychotic-disorders.

ABBREVIATIONS

AIDS : Acquired Immunodeficiency Syndrome
ACTH : Adrenocorticotropic Hormone
AVP : Arginine Vasopressin
BBB : Blood-Brain Barrier
BSI : Bloodstream Infection
CKD : Chronic Kidney Disease
COPD : Chronic Obstructive Pulmonary Diseases
COVID-19 : Coronavirus Disease 2019
CRH : Corticotropin-releasing Hormone
DNA : Deoxyribonucleic Acid
EPA : Eicosapentaenoic Acid
EGCG : Epigallocatechin Gallate
GABA : Gamma aminobutyric Acid
HAND : HIV-associated Neurocognitive Disorders
HIV : Human Immunodeficiency Virus
HPA : Hypothalamic-pituitary-adrenal Axis
IBD : Inflammatory Bowel Disease
IFN : Interferon-alpha/beta/gamma (IFN-α, IFN-β and IFN-γ)
IL-1 : Interleukin-1
IL-1β : Interleukin-1 Beta
IL-2 : Interleukin-2
IL-6 : Interleukin-6
IL-10 : Interleukin-10
IL-12 : Interleukin-12
IL-17 : Interleukin-17
IL-23 : Interleukin-23
NK : Natural killer cells
NAC : N-Acetylcysteine
NF-Kb : Nuclear factor kappa-light-chain-enhancer of Activated B Cells
PSTD : Post-traumatic Stress Disorder
ROS : Reactive oxygen Species
RNS : Reactive Nitrogen Species
Treg : Regulatory T
RA : Rheumatoid Arthritis
SLE : Systemic Lupus Erythematosus
Th1 : T helper type 1
Th17 : T helper type 17
TGF-β : Transforming Growth Factor-beta
TNF : Tumor Necrosis Factor
TNF-α : Tumor Necrosis Factor-alpha
T1D : Type 1 Diabetes
UTIs : Urinary Tract INFECTIONS
5-HT : 5-hydroxytryptamine

1. INTRODUCTION

Inflammation is a vital component of the body's immune response, playing a critical role in the defense against infections and injuries (Chen et al., 2018; Yeung et al., 2018). However, chronic inflammation has been increasingly implicated in a wide range of diseases beyond infections, including autoimmune conditions, cardiovascular disorders, and neurodegenerative diseases (Chen et al., 2018; Wang et al., 2020; Yeung et al., 2018). Recent research has also highlighted the complex interplay between inflammatory pathways and psychiatric conditions such as depression, anxiety, and schizophrenia (Miller & Raison, 2016). Studies have found that individuals with chronic inflammation, chronic infection are at a higher risk of developing depression (Chen et al., 2018; Miller & Raison, 2016; Wang et al., 2020; Yeung et al., 2018). These findings suggest that inflammation may serve as a common mechanistic link between infections, chronic diseases, and mental health disorders (Chen et al., 2018; Miller & Raison, 2016; Wang et al., 2020; Yeung et al., 2018). This review seeks to explore the multifaceted role of inflammation in the onset and progression of these conditions and underscores the necessity for integrated therapeutic approaches to address the multifaceted impact of inflammation across diverse medical disciplines.

Aims: By examining the pathways that connect infectious agents, chronic illnesses, and psychiatric disorders, we aim to provide a comprehensive understanding of how inflammation acts as a biological bridge between these seemingly disparate areas of health. The review also discusses emerging therapeutic strategies that target inflammation, highlighting their potential to transform the treatment landscape for both physical and mental health conditions. Understanding these inflammatory pathways is crucial, as it offers the opportunity to develop more holistic approaches to treating patients who suffer from a combination of physical and mental health conditions. In light of the growing global burden of chronic diseases and psychiatric disorders, a deeper insight into inflammation's role could lead to significant advancements in healthcare, improving outcomes across various domains of medicine.

1.1 Major Inflammatory cytokines

The immune system’s response to infections often triggers inflammation (Chen et al., 2018; Miller & Raison, 2016; Wang et al., 2020; Yeung et al., 2018). Inflammatory cytokines play a significant role not only in acute infections but also in the development and progression of chronic diseases (Chen et al., 2018; Miller & Raison, 2016; Wang et al., 2020; Yeung et al., 2018). In many chronic conditions, the immune system is dysregulated, leading to persistent inflammation that damages tissue and contributes to disease pathology. Some major key inflammatory cytokines involved in various chronic diseases, infection and neurological disorders are discussed in this review.

Interleukin-1 (IL-1) is a potent pro-inflammatory cytokine that enhances/boost the immune system (Henderson & Goldbach-Mansky, 2010), stimulate the production of other inflammatory cytokines, and induces fever (Henderson & Goldbach-Mansky, 2010). IL-1 plays an important role in joint degeneration and inflammation by stimulating osteoclast activity, which breaks down bone (Kim et al., 2009; Murakami et al., 2020; Ruscitti et al., 2018). IL-1 promotes chronic arterial inflammation, which contributes to the formation of plaques in arteries, leading to heart disease such as atherosclerosis (Abbate et al., 2020; Herder et al., 2015; Ridker & Rane, 2021). Chronic low-grade inflammation driven by IL-1 has been linked to insulin resistance and pancreatic beta-cell malfunction in type 2 diabetes (Herder et al., 2015; Ruscitti et al., 2018). IL-1 is produced by macrophages, neutrophils, and other immune cells. It increases the expression of adhesion molecules, which allows immune cells to migrate to sites of infection (Declercq et al., 2022; Ralph et al., 2021). It also induces fever by stimulating the hypothalamus. IL-1 is crucial for initiating acute inflammatory reaction and it plays an important role in bacterial and viral infections (Declercq et al., 2022; Ralph et al., 2021). Interleukin-1 Beta (IL-1β) is a key mediator of the inflammatory response, including fever and the synthesis of acute-phase proteins. Elevated IL-1β has been associated to both acute and chronic stages of schizophrenia (Shibuya et al., 2014; Williams et al., 2022; Zhao et al., 2023). IL-1β play a significant role in neuro-inflammation (Elenkov et al., 2000; Williams et al., 2022), and alter neurotransmitter systems dopamine implicated in psychosis (Elenkov et al., 2000; Williams et al., 2022).

Interleukin-2 (IL-2): The cytokine interleukin-2 (IL-2) is essentially for the proliferation and survival of T_{reg} in the peripheral lymphatic tissues and hence plays an important role in their

biology. Most autoimmune and rheumatic diseases (Grasshoff et al., 2021) demonstrate changes in T_{reg} biology either numerically or functionally, resulting in an imbalance between protective and pathogenic immune cells such as type 1 diabetes (T1D) and systemic lupus erythematosus (SLE) (Mizui, 2019). In several autoimmune diseases, a relative deficiency of IL-2 develops during disease pathogenesis causing a disruption of T_{reg} homeostasis, which further accelerates the vicious cycle of tolerance breach and chronic inflammation (Grasshoff et al., 2021; Moorman et al., 2021). Tumor necrosis factor (TNF) and IL-2 have been employed as a measurable immunological parameter in vaccine studies, representing vaccine activity and potentially predicting protection against *Mycobacterium tuberculosis (*Bhatt et al., 2015). The recent identification and characterization of a small population of regulatory T (T_{Reg}) cells resident in the brain presents one such potential therapeutic target (Yshii et al., 2022). IL-2 dysregulation has been reported in psychotic patients (Williams et al., 2022), with studies showing both elevated and decreased levels in schizophrenia (Huang et al., 2022; Williams et al., 2022). This variability may be related to illness stage or individual differences in immune function.

Interleukin-6 (IL-6): has both pro-inflammatory and anti-inflammatory roles, depending on the context. It induces acute-phase protein production and plays a role in T cell activation. IL-6 is a key player in joint inflammation and bone destruction in RA (Diaz-Gonzalez & Hernandez-Hernandez, 2023; Pandolfi et al., 2020). Elevated IL-6 levels are linked to chronic inflammation in blood vessels and the development of cardiovascular diseases (Abbate et al., 2020; Ridker & Rane, 2021). IL-6 contributes to insulin resistance in diabetes and obesity and is linked to chronic inflammation (Rose-John, 2021) in adipose tissue (Akbari & Hassan-Zadeh, 2018), which exacerbates metabolic disorders (Akbari & Hassan-Zadeh, 2018; Qu et al., 2014). IL-6 promotes tumor growth and survival in various cancers (Orange et al., 2023; Weber et al., 2021), including breast and prostate cancers and can serve as a negative prognostic marker in cancer, this cytokine is also involved in T cell activation (Orange et al., 2023; Rose-John, 2021; Weber et al., 2021). In the diagnosis of bloodstream infection (BSI), various inflammatory markers including IL-6, has been extensively established and can be used as a biomarker for diagnosis of infection (Yang et al., 2023). There was significantly upregulated IL-6 and IL-10 expression in the gram negative bacterial (Zhu et al., 2022). Interleukin-6 (IL-6) is a pro-inflammatory cytokine involved in the acute-phase immune response. Elevated levels of IL-6 have been consistently reported in the blood of individuals with schizophrenia (Al-Musawi et al., 2022; Patlola et al., 2023) and first-episode psychosis (Williams et al., 2022). High IL-6 is associated with cognitive deficits and may correlate with the severity of symptoms, such as hallucinations and delusions (Al-Musawi et al., 2022; Patlola et al., 2023).

Interleukin-10 (IL-10) is an anti-inflammatory cytokine/multifunctional cytokine with diverse effects on most hemopoietic cell types that limits immune responses and prevents excessive tissue damage by dampening the production of pro-inflammatory cytokines (Moore et al., 2001; Wang et al., 2019). While IL-10 limits excessive inflammation, members of the interleukin (IL)-10 family of cytokines play important roles in regulating immune responses during host defense but also in autoimmune disorders, inflammatory diseases, lupus (where the body's immune system attacks its own tissues) and cancer (Biswas et al., 2022; Mannino et al., 2015; Moore et al., 2001; Wang et al., 2019). IL-10 is an anti-inflammatory cytokine that regulates and dampens the immune response to prevent excessive inflammation and tissue damage. While IL-10 limits damage caused by inflammation, it can sometimes suppress the immune response too much, allowing chronic infections to persist if produced excessively. Current research on the microbiome of humans and other species is revealing a fundamental role in the interaction between the microbiota and the immune system in determining the health status of the host. In these studies, the cytokine interleukin-10 (IL-10) is emerging as an important player (Levast et al., 2015). IL-10 is an anti-inflammatory cytokine that helps regulate the immune response by inhibiting pro-inflammatory cytokines. Decreased levels of IL-10 have been found in individuals with schizophrenia, suggesting a failure of compensatory anti-inflammatory mechanisms (Arabska et al., 2022). Also, recent study provides new insights into the complex interplay between anti-inflammatory cytokines and generalized anxiety disorder (GAD) pathogenesis, suggesting that IL-10 may be associated with the pathophysiology and development of GAD (Sarmin et al., 2024).

Interleukin-12 (IL-12) and Interleukin-23 (IL-23): IL-12 and IL-23 are produced by antigen-presenting cells, such as dendritic cells and macrophages, and play a role in promoting Th1 and Th17 immune responses, respectively. IL-12 and IL-23 are involved in driving intestinal inflammation in Crohn's disease, inflammatory bowel disease and cancers (Aggeletopoulou et al., 2018; Tesmer et al., 2008; Verstockt et al., 2023) by promoting Th1 and Th17 immune responses (Aggarwal et al., 2003). IL-23 is involved in the pathogenesis of psoriasis by promoting Th17 cell differentiation, which enhances chronic skin inflammation (Tesmer et al., 2008; Zwicky et al., 2021). IL-12 produced by dendritic cells and macrophages, IL-12 promotes the differentiation of T cells into Th1 cells, which are essential for fighting intracellular pathogens. IL-12 bridges innate and adaptive immunity and is crucial for controlling viral and bacterial infections by promoting a Th1 immune response (Novelli & Casanova, 2004; Wozniak et al., 2006). Interleukin-12 (IL-12) and Interleukin-23 (IL-23) are pro-inflammatory cytokines that play important roles in immune system regulation. Increasing evidence suggests that these cytokines may also be involved in the pathophysiology of psychotic disorders, such as schizophrenia. IL-12 is primarily involved in the differentiation of naive T cells into Th1 cells, which produce interferon-gamma (IFN-γ), a pro-inflammatory cytokine. Dysregulation of the Th1 immune response has been implicated in neuro-inflammatory processes seen in schizophrenia and other psychotic disorders. IL-23 promotes the differentiation and maintenance of Th17 cells, which are implicated in autoimmune and inflammatory responses. Th17 cells produce IL-17, another pro-inflammatory cytokine that has been associated with psychiatric conditions (Wozniak et al., 2006).

Interleukin-17 (IL-17): IL-17 is produced by a subset of T cells called Th17 cells (Aggarwal et al., 2003). It promotes inflammation by stimulating the production of other pro-inflammatory cytokines and recruiting neutrophils (Aggarwal et al., 2003; Ergen & Yusuf, 2018). IL-17 is a key mediator of skin inflammation, leading to the thickened, scaly patches characteristic of psoriasis (Ergen & Yusuf, 2018; Zwicky et al., 2021). IL-17 is involved in joint inflammation and destruction by enhancing the activity of other pro-inflammatory cytokines and contributing to bone erosion in RA. IL-17 contributes to the inflammatory damage of the central nervous system, leading to the neurological symptoms of multiple sclerosis (Ergen & Yusuf, 2018). Interleukin-17 (IL-17) is a pro-inflammatory cytokine primarily produced by Th17 cells, a subset of T-helper cells. Its role in psychotic disorders, including schizophrenia and bipolar disorder, has been increasingly investigated as part of the broader understanding of immune system dysregulation in mental health conditions. Elevated levels of IL-17 have been found in patients with schizophrenia and other psychotic disorders, suggesting that IL-17 may play a role in the immune-inflammatory mechanisms contributing to these conditions.

Interferon-gamma (IFN-γ) is produced by T cells and natural killer (NK) cells and is involved in activating macrophages, enhancing their ability to destroy pathogens. In Autoimmune diseases, IFN-γ is implicated in the pathogenesis of autoimmune diseases like multiple sclerosis (MS), type 1 diabetes, and systemic lupus erythematosus (SLE). It enhances immune responses that mistakenly target the body's own tissues. In chronic infections such as tuberculosis or viral hepatitis, IFN-γ helps control the infection but can also contribute to tissue damage through prolonged activation of immune cells. IFN-γ is a type II interferon produced mainly by T cells and natural killer (NK) cells. It activates macrophages, enhancing their ability to kill ingested pathogens, and promotes antigen presentation. IFN-γ is crucial for defense against intracellular pathogens such as viruses and certain bacteria (e.g., Mycobacterium tuberculosis). Interferon-alpha/beta (IFN-α and IFN-β): These are type I interferons primarily involved in antiviral defense. They are produced by virus-infected cells and help in inhibiting viral replication and activating NK cells (Zhao et al., 2024). IFN-α and IFN-β are essential for controlling viral infections by enhancing the antiviral state of surrounding cells and stimulating immune cell activity (Zhao et al., 2024). IFN-α is used as a therapeutic agent in certain viral infections (e.g., hepatitis C) and some cancers. However, treatment with IFN-α is often associated with neuropsychiatric side effects, including depression, anxiety, and even psychosis. This suggests that interferons may have a direct effect on brain function (Zhao et al., 2024).

Transforming Growth Factor-beta (TGF-β): TGF-β has both pro-inflammatory and anti-inflammatory roles depending on the context. It is involved in tissue repair, immune suppression,

and the regulation of other immune responses. In diseases such as pulmonary fibrosis, liver cirrhosis, and chronic kidney disease (Budi et al., 2021), TGF-β promotes excessive tissue repair and the deposition of extracellular matrix, leading to tissue scarring and organ dysfunction (Budi et al., 2021; Hourani et al., 2024). TGF-β can contribute to cancer progression by promoting tumor cell invasion, immune evasion, and metastasis (Budi et al., 2021; Hourani et al., 2024). TGF-β is involved in the regulation of immune responses. In some autoimmune conditions, its dysregulation can contribute to inflammation and tissue damage. For instance, in rheumatoid arthritis and lupus, TGF-β can promote the activation of pathogenic immune cells (Li et al., 2006). In the context of psychotic disorders, such as schizophrenia, TGF-β has emerged as a molecule of interest due to its involvement in neuroinflammation, neurodevelopment, and synaptic plasticity (Adamu et al., 2024; Kolliker-Frers et al., 2021). TGF-β generally acts as an anti-inflammatory cytokine by suppressing pro-inflammatory responses in the brain (Adamu et al., 2024; Kolliker-Frers et al., 2021). Chronic inflammation and immune dysregulation are thought to play significant roles in the pathophysiology of psychotic disorders, especially schizophrenia (Adamu et al., 2024; Kolliker-Frers et al., 2021). Lower levels of TGF-β have been associated with increased inflammation in the brain, which may contribute to the development of psychotic symptoms (Adamu et al., 2024; Kolliker-Frers et al., 2021). Dysregulation of TGF-β signaling could lead to overactivation of microglia, contributing to neuroinflammation in psychotic disorders (Adamu et al., 2024; Kolliker-Frers et al., 2021).

Tumor Necrosis Factor-alpha (TNF-α): TNF-α is a pro-inflammatory cytokine primarily produced by macrophages (Idriss & Naismith, 2000), it plays a central role in inflammation by promoting the activation of immune cells and the expression of other inflammatory molecules (Balkwill, 2006; Chen et al., 2018; Idriss & Naismith, 2000; Jang et al., 2021; Lanka et al., 2024). TNF-α promotes the inflammation of joints, leading to pain, swelling, and destruction of cartilage and bone rheumatoid arthritis (RA). Overproduction of TNF-α is linked to chronic inflammation in the gut, contributing to inflammatory bowel diseases like Crohn's disease, ulcerative colitis and other autoimmune diseases (Balkwill, 2006; Jang et al., 2021). TNF-α contributes to lung inflammation and tissue destruction resulting to obstructive pulmonary diseases (COPD). TNF-α promotes chronic skin inflammation and excessive skin cell proliferation in psoriasis (Li et al., 2019). TNF-α promotes inflammation by inducing fever, increasing vascular permeability, and recruiting immune cells to the site of infection (Dorhoi & Kaufmann, 2014). It helps in controlling infections by stimulating the immune response but can also cause tissue damage if overproduced, contributing to conditions like septic shock (Georgescu et al., 2020). TNF-α is another pro-inflammatory cytokine that plays a crucial role in systemic inflammation and immune regulation (Georgescu et al., 2020). Increased TNF-α levels have been found in patients with schizophrenia and bipolar disorder (Hope et al., 2013; Millett et al., 2020). Elevated TNF-α may contribute to neurodegenerative processes observed in these disorders by promoting oxidative stress and apoptosis (Hope et al., 2013; Millett et al., 2020).

2. HPA AXIS DYSREGULATION

The hypothalamic-pituitary-adrenal (HPA) axis plays a crucial role in the body's response to stress (McEwen, 2007). Chronic activation of this system, often seen in response to infections and chronic diseases (Chang, 2011), can result in an overproduction of cortisol, elevated cortisol levels have been linked to psychiatric disorders like depression, anxiety, and PTSD (Hewagalamulage et al., 2016; McEwen, 2007; O'Connor et al., 2020). Severe infections can cause prolonged activation of the HPA axis, leading to stress-related psychiatric symptoms. Conditions like metabolic syndrome and cardiovascular disease are known to dysregulate the HPA axis (Chang, 2011). Overactivation of the HPA axis, commonly seen in depression and anxiety, increases stress responses, which worsen psychiatric symptoms (McEwen, 2007; O'Connor et al., 2020). The hypothalamic-pituitary-adrenal (HPA) axis in infection is a major neuroendocrine system that plays a crucial role in the body's response to stress, including during infection. It involves interactions between the hypothalamus, pituitary gland, and adrenal glands and leads to the secretion of hormones, such as cortisol, which helps modulate the immune response. When the body detects an infection, immune cells release pro-inflammatory cytokines, these cytokines signal the hypothalamus to activate the HPA axis. The hypothalamus responds by secreting corticotropin-releasing hormone (CRH) and

arginine vasopressin (AVP) (Papadimitriou & Priftis, 2009; Sukhareva, 2021). These hormones stimulate the pituitary gland and then releases adrenocorticotropic hormone (ACTH), which travels through the bloodstream to the adrenal glands that produces and releases cortisol, a glucocorticoid hormone, in response to ACTH (Chen et al., 2018; Papadimitriou & Priftis, 2009; Sukhareva, 2021). Dysregulation of the HPA axis plays a significant role in psychotic disorders (Chan et al., 2010; Mikulska et al., 2021; Murphy et al., 2022). Major depression is associated with hyperactivation of the HPA axis and elevated cortisol levels, which can worsen both psychological and physical symptoms in patients with chronic illness (Chan et al., 2010; Mikulska et al., 2021; Murphy et al., 2022). Dysregulation of this axis has been extensively studied in the context of psychotic disorders, especially schizophrenia. Many studies have reported elevated levels of cortisol in individuals with psychotic disorders, particularly during acute phases of illness, indicating hyperactivity of the HPA axis (Chan et al., 2010; Mikulska et al., 2021; Murphy et al., 2022).

3. NEUROINFLAMMATION

Neuroinflammation, chronic diseases, and infections share several common pathways, particularly in the context of immune responses, signaling cascades, and cellular processes that contribute to disease progression. In the brain, microglial cells (resident immune cells) become activated during neuroinflammation, producing pro-inflammatory cytokines and reactive oxygen species (ROS) (Adamu et al., 2024; Andronie-Cioara et al., 2023; Ly et al., 2023). Chronic activation of microglia is a hallmark of neurodegenerative diseases such as Alzheimer's and Parkinson's (Adamu et al., 2024; Andronie-Cioara et al., 2023; Ly et al., 2023). In chronic diseases and infections (Adamu et al., 2024), macrophages also become activated, releasing inflammatory mediators and contributing to tissue damage, fibrosis, and systemic inflammation (Adamu et al., 2024; Ly et al., 2023).

The overproduction of ROS and reactive nitrogen species (RNS) leads to cellular damage, DNA mutations, and protein degradation (Wadhwa et al., 2018; Zarkovic, 2020). This is a common pathway in neuroinflammation (Wadhwa et al., 2018), chronic diseases (e.g., atherosclerosis, diabetes) (Jomova et al., 2023), and during infections (Zarkovic, 2020). ROS-induced damage can result in neurodegeneration (e.g., Alzheimer's) (Wadhwa et al., 2018) and systemic complications (e.g., in diabetes or chronic infections like HIV) (Zarkovic, 2020). NF-κB Pathway is a key regulator of the immune response to infection (Poladian et al., 2023), inflammation, and cellular stress (Baker et al., 2011; Zarkovic, 2020). It controls the transcription of genes involved in inflammation, immune responses, and cell survival. Persistent activation of NF-κB is associated with chronic inflammatory diseases (like rheumatoid arthritis, inflammatory bowel disease) (Baker et al., 2011; Jomova et al., 2023) and neuroinflammatory condition. Dysfunctional mitochondria are sources of ROS, contributing to oxidative stress and inflammation. Mitochondrial damage is a feature of neurodegenerative diseases (Wadhwa et al., 2018) and is also implicated in chronic conditions such as type 2 diabetes and cardiovascular diseases (Jomova et al., 2023). In infections, pathogens can directly target mitochondria to manipulate host cell responses, further enhancing inflammation (Andrieux et al., 2021; Foo et al., 2022; Poladian et al., 2023).

Blood-Brain Barrier (BBB) Disruption. In neuroinflammation, BBB integrity is often compromised, allowing peripheral immune cells, cytokines, and pathogens to infiltrate the brain, exacerbating inflammation (Mapunda et al., 2022; Sanmarco et al., 2021). This is seen in conditions like encephalitis, multiple sclerosis, and systemic infections like sepsis (Haruwaka et al., 2019; Ortiz et al., 2014). Chronic diseases such as hypertension and diabetes can also disrupt BBB function, contributing to neuroinflammation (Mapunda et al., 2022; Mayer & Fischer, 2024; Michalicova et al., 2020; Sanmarco et al., 2021).

Inflammasome Activation: NLRP3 inflammasome is a protein complex that becomes activated in response to cellular stress, infection, and metabolic disturbances (Fu & Wu, 2023; Han et al., 2023; Li et al., 2023; Liu et al., 2018). It plays a central role in producing various cytokines which are key mediators of inflammation (Li et al., 2023). Dysregulation of the inflammasome is implicated in neuroinflammatory diseases (e.g., Alzheimer's) as well as chronic metabolic conditions like obesity, type 2 diabetes and in various infections (Alonaizan, 2024; Han et al., 2023; Li et al., 2023; Xu et al., 2019).

Gut-Brain Axis and Systemic Inflammation. Disruptions in the gut microbiome can lead to systemic inflammation, which in turn can affect brain function and contribute to neuroinflammation (Mou et al., 2022; Zhao et al., 2021). This link is seen in diseases like multiple sclerosis, depression, and chronic infections. The gut-brain axis is a key pathway in both chronic systemic diseases like inflammatory bowel disease and neuroinflammatory processes (Mou et al., 2022; Ruze et al., 2023; Zhao et al., 2021).

4. PSYCHIATRIC SYMPTOMS ASSOCIATED WITH INFECTION AND CHRONIC DISEASES

Depression: Depression is one of the most common psychiatric conditions in individuals with infection and chronic diseases such as HIV/AIDS, COVID-19, tuberculosis, Cancer, and cardiovascular diseases (Gazdag et al., 2014; Munjal et al., 2017). It can result from the emotional stress of living with a chronic illness, social stigma, and the neurological impact of the microorganisms itself (Gazdag et al., 2014; Munjal et al., 2017).

Anxiety: Anxiety disorders, including generalized anxiety disorder, panic disorder, and post-traumatic stress disorder (PTSD), are prevalent among those with cancer, COVID-19, HIV/AIDS and related heart diseases (Gazdag et al., 2014; Munjal et al., 2017). Concerns about health, finance, relationships, societal stigma, and future uncertainties contribute to these feelings.

Cognitive Impairment: HIV-associated neurocognitive disorders (HAND) can range from mild cognitive decline to severe dementia (Gazdag et al., 2014; Munjal et al., 2017). Cognitive impairments can affect memory, concentration, and decision-making abilities, impacting daily functioning (Gazdag et al., 2014; Munjal et al., 2017).

5. PROSPECTIVE THERAPEUTIC APPLICATIONS IN MENTAL DISORDERS, INFECTION AND CHRONIC DISEASES

Probiotic and mental disorders: A probiotic is a live organism that, when ingested in adequate amounts, exerts a health benefit (Kim et al., 2019). Gut microflora can also be balanced by directly adding live microorganisms into the diet. The genera and species that have been used are *Lactobacillus, Streptococcus, Leuconostoc, Pediococcus, Propionibacterium, Enterococcus, Bifidobacterium, Bacillus, Saccharomyces cerevisiae, Candida pintolopesii, Aspergillus niger* and *A. oryzae (*Kim et al., 2019*)*. Their use in mental illness has been reviewed more extensively elsewhere (Dicks, 2022; Dicks et al., 2021). Several members of the microbiota are known to produce neurotransmitters such as dopamine, gamma aminobutyric acid (GABA), norepinephrine, serotonin (5-HT), acetylcholine, and endocannabinoids (Dicks, 2022; Dicks et al., 2021). This, together with the finding that ingestion of *Bifidobacterium infantis* in rats increases the levels of tryptophan (Desbonnet et al., 2008), supports the hypothesis that the microbiota plays a role in the modulation of neurotransmitter levels and possibly also mood (Desbonnet et al., 2008; Dicks, 2022; Dicks et al., 2021).

Probiotics and chronic diseases: Probiotics, beneficial live microorganisms, are increasingly studied for their role in managing chronic diseases (Yadav et al., 2022). Their primary application involves restoring and maintaining a balanced gut microbiome, which is critical for immune function, metabolism, and inflammation regulation (Yadav et al., 2022). In chronic diseases like chronic kidney disease and inflammatory bowel disease (IBD) (Cooper et al., 2023; Ewaschuk & Dieleman, 2006), probiotics can help reduce inflammation and promote intestinal healing (Cooper et al., 2023; Ewaschuk & Dieleman, 2006; Yadav et al., 2022; Zhu et al., 2021). For cardiovascular disease, they may improve lipid profiles by lowering cholesterol levels (Singh et al., 2017; Yadav et al., 2022). In diabetes, probiotics aid in regulating blood glucose by enhancing insulin sensitivity. They also show promise in managing obesity, non-alcoholic fatty liver disease (Shen et al., 2024; Singh et al., 2017; Yadav et al., 2022).

Probiotics and infection: Probiotics play a promising role in managing and preventing infectious diseases (Adeniyi et al., 2024; Darbandi et al., 2021). They help restore the balance of gut microbiota, which can be disrupted during infections or antibiotic treatments (Adeniyi et al., 2024; Li et al., 2022; Tegegne & Kebede, 2022; Yadav et al., 2022). Probiotics such as *Lactobacillus* and *Bifidobacterium* species are particularly effective against gastrointestinal infections like *Clostridium difficile*, *Helicobacter pylori*, *Salmonella* spp and acute diarrhea caused by

viral or bacterial pathogens in human (Adeniyi et al., 2024; Adeniyi et al., 2015; Li et al., 2022; Tegegne & Kebede, 2022; Yadav et al., 2022) and animals (Adetoye et al., 2018; Adeniyi and Olorunnisola, 2024). They work by enhancing the gut's natural barrier, modulating immune responses, and competing with pathogens for adhesion sites and nutrients. In respiratory infections, some studies suggest probiotics can reduce the severity and duration of symptoms by strengthening immune defenses. They also show potential in preventing urinary tract infections (UTIs) by inhibiting pathogen colonization in the urogenital tract (Adeniyi et al., 2024; Li et al., 2022; Tegegne & Kebede, 2022; Yadav et al., 2022).

6. NATURAL PRODUCT

The use of natural products in managing psychotic disorders has garnered interest due to their potential benefits and fewer side effects compared to conventional antipsychotic medications (Hoenders et al., 2018; Kulamarva et al., 2023; Saleem et al., 2022). While research on natural remedies is still emerging, several herbs, nutrients, and supplements have shown promise for supporting mental health and may complement standard treatments for psychosis, schizophrenia, anxiety/depression, or related condition (Hoenders et al., 2018; Kulamarva et al., 2023; Saleem et al., 2022).

Natural products, derived from plants, animals, and microorganisms, have been extensively used in the management of infectious diseases for centuries (Chopra & Dhingra, 2021; Dias et al., 2012; Jugran et al., 2021). They offer a diverse array of bioactive compounds that can serve as alternatives or complements to synthetic drugs, particularly in an era of rising antimicrobial resistance (Chopra & Dhingra, 2021; Dias et al., 2012; Jugran et al., 2021). Examples: Alkaloids (e.g., berberine from Berberi's species): Possess broad-spectrum antibacterial activity. Flavonoids (e.g., quercetin): Inhibit bacterial growth by targeting bacterial enzymes. Essential oils (e.g., tea tree oil, oregano oil): Effective against Gram-positive and Gram-negative bacteria (Khare et al., 2021; Othman et al., 2019). Curcumin (from turmeric): Can reverse antibiotic resistance in some strains by interfering with bacterial resistance mechanisms (Dai et al., 2022; Hussain et al., 2022). Natural products have long been used in the management of chronic diseases due to their wide range of bioactive compounds, which often have therapeutic effects (Kroth et al., 2021; Puri et al., 2022; Rios et al., 2015). These products, derived from plants, animals, and microorganisms, can act as antioxidants, anti-inflammatory agents, immune modulators, in the management of mental health (Cortez-Navarrete et al., 2023) or even target specific metabolic pathways.

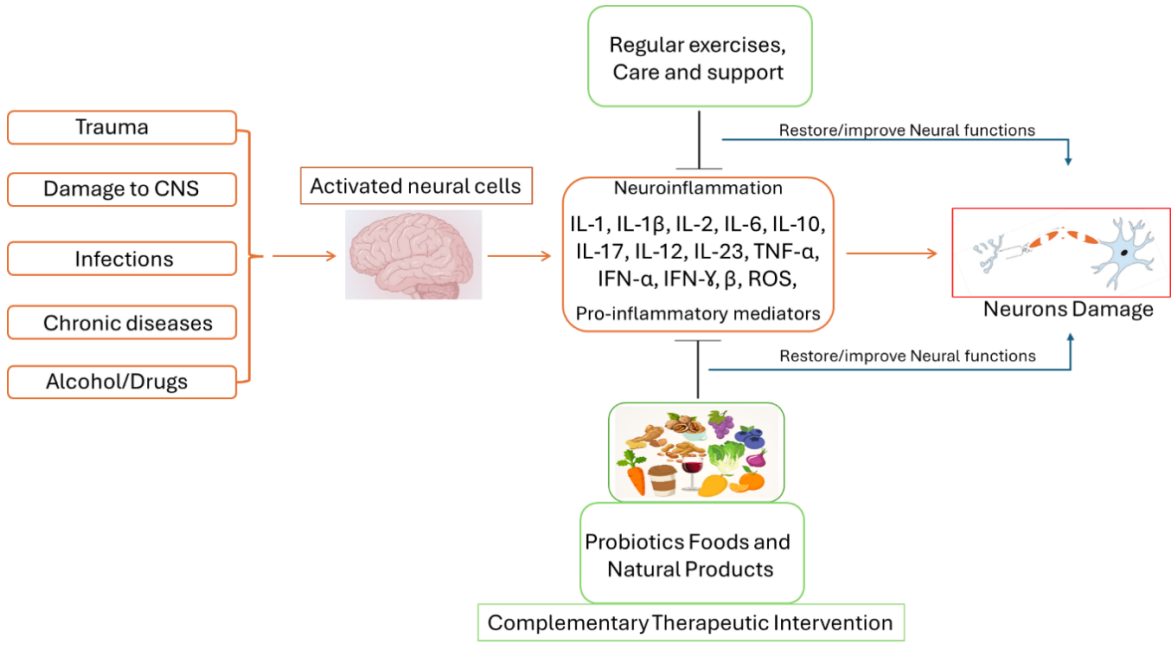

Fig .1. Therapeutic Applications in Mental Disorders

Table 1. Natural products and functions in management of depression/anxiety/psychotic disorders

	Natural product/Sources	Function	Ref
Psychotic disorders	Omega-3 Fatty Acids	Omega-3 fatty acids, particularly eicosapentaenoic acid (EPA), have anti-inflammatory effects and may help improve mood, cognitive function, and reduce the severity of psychotic symptom	(Bozzatello et al., 2016) (Gow & Hibbeln, 2014) (Hsu et al., 2020)
	Extract from the Ginkgo biloba tree	Ginkgo biloba is believed to improve blood flow to the brain and has antioxidant properties. It may help in reducing the cognitive symptoms of schizophrenia when used as an adjunct to antipsychotic medications.	(Singh et al., 2010) (Chandrasekaran et al., 2001) (Doruk et al., 2008)
	Curcumin (Turmeric)	Curcumin, the active compound in turmeric, has anti-inflammatory and antioxidant properties. It is thought to modulate neurotransmitter pathways and reduce inflammation in the brain, which may play a role in managing psychosis	(El-Saadony et al., 2022) (Spanoudaki et al., 2024) (Adeniyi et al., 2024)
	N-Acetylcysteine (NAC)	NAC is a precursor to glutathione, an antioxidant that reduces oxidative stress in the brain. Studies have shown that NAC may help alleviate symptoms of schizophrenia, including negative symptoms such as social withdrawal, and improve overall functioning.	(Dean et al., 2011) (Lane et al., 2008)
	Passionflower (*Passiflora incarnata*)	Passionflower has been traditionally used to treat anxiety and insomnia, which are often comorbid with psychosis. It may have mild sedative properties, helping with agitation or sleep disturbances	(Janda et al., 2020) (da Fonseca et al., 2020)
		Valerian root is often used as a sleep aid and for reducing anxiety. Since sleep disturbances and anxiety can exacerbate psychotic symptoms, valerian may help	(Tammadon et al., 2021)

	Natural product/Sources	Function	Ref
	Valerian Root	improve these secondary symptoms.	(Sahin et al., 2024)
	Saffron (*Crocus sativus*)	Saffron has been traditionally used to improve mood and has shown potential in treating depression and anxiety. Given its neuroprotective and anti-inflammatory effects, it may provide adjunctive support in treating negative symptoms in psychotic disorders.	(Bian et al., 2020) (Omidkhoda & Hosseinzadeh, 2022) (Shafiee et al., 2018)
	B Vitamins (e.g., B6, B12, Folate). Found in whole grains, leafy greens, meats, and fortified foods.	B vitamins play a critical role in brain function, particularly in producing neurotransmitters like serotonin and dopamine. Deficiencies in B vitamins, especially folate and B12, have been linked to cognitive and mental health problems, and supplementation may help reduce the severity of psychotic symptoms.	(Kale et al., 2010) (Hoffer, 2008)

Table 2. Natural products and functions in management of metabolic diseases.

	Natural product/Sources	Function	Ref
Diabetes	Cinnamon, Bitter melon and Fenugreek	Contains fibers and soluble compounds that may improve insulin sensitivity and lower blood sugar levels	(Verma et al., 2016)
Cardiovascular Disease	Garlic	Garlic: Known for its ability to reduce blood pressure and improve cholesterol levels.	(Ried, 2020) (Banerjee & Maulik, 2002)
	Omega-3 fatty acids	Omega-3 Fatty Acids (Fish Oil): Help lower triglycerides, reduce inflammation, and improve heart function.	(Zivkovic et al., 2011) (Shearer et al., 2012)
	Flavonoids	Flavonoids (from berries, green tea, dark chocolate): Act as antioxidants and help	(Grassi et al., 2010)

	Natural product/Sources	Function	Ref
		improve endothelial function, thus reducing the risk of CVD	(Rees et al., 2018)
Cancer	Curcumin	Curcumin (Turmeric): Has anti-inflammatory and antioxidant properties and may inhibit the growth of cancer cells.	(Zoi et al., 2021) (Singh et al., 2011)
	Green Tea	Green Tea (EGCG): Contains epigallocatechin gallate, which has been shown to suppress tumor growth and improve the body's detoxification process.	(Jang et al., 2022) (Florio et al., 2023)
	Resveratrol	Resveratrol (Grapes, Red Wine): Acts as an antioxidant and has anti-cancer properties by inhibiting cancer cell proliferation.	Karabekir & Ozgorgulu, (2020)
Arthritis and Joint Disorders	Glucosamine /Chondroitin	Glucosamine and Chondroitin: Commonly used supplements for osteoarthritis to reduce joint pain and improve mobility.	(Zhu et al., 2018)
	Boswellia	Boswellia: A herbal extract with anti-inflammatory properties, often used to reduce symptoms of osteoarthritis and rheumatoid arthritis.	(Siddiqui, 2011)
	Omega-3 fatty acids	Omega-3 Fatty Acids: Also play a role in reducing joint inflammation in rheumatoid arthritis.	(Goldberg & Katz, 2007)
Chronic Inflammatory Condition	Ginger	Ginger: Has anti-inflammatory and analgesic properties, used to manage conditions like osteoarthritis and digestive inflammation.	(Szymczak et al., 2024)
	Turmeric	Turmeric: Reduces chronic inflammation and is used in conditions such as inflammatory bowel disease (IBD) and arthritis.	(He et al., 2015) (Bahrami et al., 2020)
	Aloe vera	Aloe Vera: Often used to soothe inflammation in skin conditions and gut disorders like ulcerative colitis	(Barton et al., 2022)
	Curcuma longa L.	*Curcuma longa* (Curcumin): significantly reduced chronic inflammation and HP-induced gastric lesions, as assessed both	(Mahady et

	Natural product/Sources	Function	Ref
	Diospyros spp	macroscopically and microscopically in *Mongolian gerbils*. Some bi-naphthoquinones from *Diospyros* sp. have anti-inflammatory activity.	al., 2006) Kuke et al, 1998
Chronic Respiratory Diseases (Asthma, COPD)	Licorice root NAC Honey	Licorice Root: Used to soothe airways and reduce inflammation in respiratory conditions. N-Acetylcysteine (NAC): A precursor to glutathione, used to thin mucus and improve lung function in COPD. Honey: Often used to soothe cough and irritation in the respiratory tract, particularly in asthma.	(Hocaoglu et al., 2011) (Sadowska et al., 2006) (Goldman, 2014)
Liver Diseases	Silymarin Dandelion root	Milk Thistle (Silymarin): Used for its hepatoprotective effects in managing liver diseases like hepatitis and cirrhosis. Dandelion Root: Known for its detoxifying properties and support for liver function.	(Vargas-Mendoza et al., 2014) (Pfingstgraf et al., 2021)
Obesity and Metabolic Syndrome	Green tea Extract Apple cider Capsaicin	Green Tea Extract: Increases fat oxidation and improves metabolic rate, helping in weight management. Apple Cider Vinegar: May help with weight loss by promoting satiety and stabilizing blood sugar levels. Capsaicin (from chili peppers): Increases energy expenditure and fat oxidation, helping in weight management.	(Roberts et al., 2021) (Abou-Khalil et al., 2024) (Zheng et al., 2017)

7. POSSIBLE SIDE EFFECTS OF NATURAL PRODUCTS

The general population believes that natural products, such as "health foods" and herbal medicines, are reliable and beneficial, nonetheless, care must be taken when using natural products. Preclinical studies have revealed that natural products can prevent or treat a variety of ailments, including cancer, cystic fibrosis, infection, and neurological disorders (Bailey & Dresser, 2004; Basaran et al., 2022; Hewlings & Kalman, 2017). Based on phase I clinical data on oral curcumin dosing at 8,000 mg/day, there have been no significant side effects other than moderate nausea and diarrhea (Hewlings & Kalman, 2017). However, excessive use of any natural substance might affect the gut flora, disrupting normal physiological and immunological processes (Bailey & Dresser, 2004; Basaran et al., 2022; Hewlings & Kalman, 2017). Furthermore, the simultaneous use of medications and some medicinal plants can have major side effects and reduce the efficacy of the therapy. When medications with a defined therapeutic index are combined with plants that can impact drug metabolizing enzymes and disturb systemic circulation, such as bioavailability or excretion, unexpected adverse effects may occur (Bailey & Dresser, 2004; Basaran et al., 2022; Hewlings & Kalman, 2017).

8. CONCLUSION

Inflammatory cytokines are crucial for initiating and regulating the immune response during infections. However, while they help clear pathogens, an excessive cytokine response can cause tissue damage and worsen the infection. Balancing cytokine activity is critical for effective immunity without causing harmful inflammation. In chronic diseases, inflammatory cytokines are key drivers of ongoing tissue damage and immune system dysfunction. These cytokines play a double-edged role: while essential for host defense and healing, their prolonged or excessive activity can contribute to disease progression.

CONSENT AND ETHICAL APPROVAL

It is not applicable.

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators have been used during the writing or editing of this manuscript.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

Abbate, A., Toldo, S., Marchetti, C., Kron, J., Van Tassell, B. W., & Dinarello, C. A. (2020). Interleukin-1 and the Inflammasome as Therapeutic Targets in Cardiovascular Disease. *Circ Res*, *126*(9), 1260-1280. https://doi.org/10.1161/CIRCRESAHA.120.315937

Abou-Khalil, R., Andary, J., & El-Hayek, E. (2024). Apple cider vinegar for weight management in Lebanese adolescents and young adults with overweight and obesity: a randomised, double-blind, placebo-controlled study. *BMJ Nutr Prev Health*, *7*(1), 61-67. https://doi.org/10.1136/bmjnph-2023-000823

Adamu, A., Li, S., Gao, F., & Xue, G. (2024). The role of neuroinflammation in neurodegenerative diseases: current understanding and future therapeutic targets. *Front Aging Neurosci*, *16*, 1347987. https://doi.org/10.3389/fnagi.2024.1347987

Adeniyi B. A. and Olorunnisola, M. M. (2024). Gut Microbiome Derived Lactic Acid Bacteria (GM-d-LAB) from Dwarf Goats (*Capra aegagrus hircus)* Inhibit the Resident Multiple Antibiotics Resistance Bacterial pathogens. Journal of Pharmaceutical Research International. 36(1) : 1-12 DOI: 10.9734/jpri/2024/v36i17492

Adeniyi GP, Igbokwe CO, Mahady GB, Adeniyi BA. 2024. The Role of Plants having Antimicrobial Properties in the Management of Mental Health Disorders: A Review. Journal of Complimentary and Alternative Medical Research 25 (11):125-46. https://doi: 10.9734/jocamr/2024/v25i11588

Adeniyi, B. A., Adetoye, A., & Ayeni, F. A. (2015). Antibacterial activities of lactic acid bacteria isolated from cow faeces against potential enteric pathogens. *Afr Health Sci*, *15*(3), 888-895. https://doi.org/10.4314/ahs.v15i3.24

Adeniyi, B., Adesuyi, A., Ayeni, F., Ogunbanwo, T., & Agidigbi, T. (2024). Poultry Gastrointestinal-derived Lactic Acid Bacteria (pGIT-d-LAB) Inhibit Multiple Antibiotics Resistance Bacterial and Fungal Pathogens. *Avicenna J Med Biotechnol*, *16*(2), 111-119. https://doi.org/10.18502/ajmb.v16i2.14862

Adetoye, A., Pinloche, E., Adeniyi, B. A., & Ayeni, F. A. (2018). Characterization and anti-salmonella activities of lactic acid bacteria isolated from cattle faeces. *BMC Microbiol*, *18*(1), 96. https://doi.org/10.1186/s12866-018-1248-y

Aggarwal, S., Ghilardi, N., Xie, M. H., de Sauvage, F. J., & Gurney, A. L. (2003). Interleukin-23 promotes a distinct CD4 T cell activation state characterized by the production of interleukin-17. *J Biol Chem*, *278*(3), 1910-1914. https://doi.org/10.1074/jbc.M207577200

Aggeletopoulou, I., Assimakopoulos, S. F., Konstantakis, C., & Triantos, C. (2018). Interleukin 12/interleukin 23 pathway: Biological basis and therapeutic effect in patients with Crohn's disease. *World J Gastroenterol*, *24*(36), 4093-4103. https://doi.org/10.3748/wjg.v24.i36.4093

Akbari, M., & Hassan-Zadeh, V. (2018). IL-6 signalling pathways and the development of type 2 diabetes. *Inflammopharmacology*, *26*(3), 685-698. https://doi.org/10.1007/s10787-018-0458-0

Al-Musawi, A. F., Al-Hakeim, H. K., Al-Khfaji, Z. A., Al-Haboby, I. H., Almulla, A. F., Stoyanov, D. S., & Maes, M. (2022). In Schizophrenia, the Effects of the IL-6/IL-23/Th17 Axis on Health-Related Quality of Life and Disabilities Are Partly Mediated by Generalized Cognitive Decline and the Symptomatome. *Int J Environ Res Public Health*, *19*(22). https://doi.org/10.3390/ijerph192215281

Alonaizan, R. (2024). Molecular regulation of NLRP3 inflammasome activation during parasitic infection. *Biosci Rep*, *44*(5). https://doi.org/10.1042/BSR20231918

Andrieux, P., Chevillard, C., Cunha-Neto, E., & Nunes, J. P. S. (2021). Mitochondria as a Cellular Hub in Infection and Inflammation. *Int J Mol Sci*, *22*(21). https://doi.org/10.3390/ijms222111338

Andronie-Cioara, F. L., Ardelean, A. I., Nistor-Cseppento, C. D., Jurcau, A., Jurcau, M. C., Pascalau, N., & Marcu, F. (2023). Molecular Mechanisms of Neuroinflammation in Aging and Alzheimer's Disease Progression. *Int J Mol Sci*, *24*(3). https://doi.org/10.3390/ijms24031869

Arabska, J., Wysokinski, A., Brzezinska-Blaszczyk, E., & Kozlowska, E. (2022). Serum Levels and in vitro CX3CL1 (Fractalkine), CXCL8, and IL-10 Synthesis in Phytohemaglutinin-Stimulated and Non-stimulated Peripheral Blood Mononuclear Cells in Subjects With Schizophrenia. *Front Psychiatry*, *13*, 845136. https://doi.org/10.3389/fpsyt.2022.845136

Bahrami, G., Malekshahi, H., Miraghaee, S., Madani, H., Babaei, A., Mohammadi, B., & Hatami, R. (2020). Protective and Therapeutic Effects of Aloe Vera Gel on Ulcerative Colitis Induced by Acetic Acid in Rats. *Clin Nutr Res*, *9*(3), 223-234. https://doi.org/10.7762/cnr.2020.9.3.223

Bailey, D. G., & Dresser, G. K. (2004). Natural products and adverse drug interactions. *CMAJ*, *170*(10), 1531-1532. https://doi.org/10.1503/cmaj.1031558

Baker, R. G., Hayden, M. S., & Ghosh, S. (2011). NF-kappaB, inflammation, and metabolic disease. *Cell Metab*, *13*(1), 11-22. https://doi.org/10.1016/j.cmet.2010.12.008

Balkwill, F. (2006). TNF-alpha in promotion and progression of cancer. *Cancer Metastasis Rev*, *25*(3), 409-416. https://doi.org/10.1007/s10555-006-9005-3

Banerjee, S. K., & Maulik, S. K. (2002). Effect of garlic on cardiovascular disorders: a review. *Nutr J*, *1*, 4. https://doi.org/10.1186/1475-2891-1-4

Barton, V. R., Toussi, A., Awasthi, S., & Kiuru, M. (2022). Treatment of pediatric alopecia areata: A systematic review. *J Am Acad Dermatol*, *86*(6), 1318-1334. https://doi.org/10.1016/j.jaad.2021.04.077

Basaran, N., Pasli, D., & Basaran, A. A. (2022). Unpredictable adverse effects of herbal products. *Food Chem Toxicol*, *159*, 112762. https://doi.org/10.1016/j.fct.2021.112762

Bhatt, K., Verma, S., Ellner, J. J., & Salgame, P. (2015). Quest for correlates of protection against tuberculosis. *Clin Vaccine Immunol*, *22*(3), 258-266. https://doi.org/10.1128/CVI.00721-14

Bian, Y., Zhao, C., & Lee, S. M. (2020). Neuroprotective Potency of Saffron Against Neuropsychiatric Diseases, Neurodegenerative Diseases, and Other Brain Disorders: From Bench to Bedside. *Front Pharmacol*, *11*, 579052. https://doi.org/10.3389/fphar.2020.579052

Biswas, S., Bieber, K., & Manz, R. A. (2022). IL-10 revisited in systemic lupus erythematosus. *Front Immunol*, *13*, 970906. https://doi.org/10.3389/fimmu.2022.970906

Bozzatello, P., Brignolo, E., De Grandi, E., & Bellino, S. (2016). Supplementation with Omega-3 Fatty Acids in Psychiatric Disorders: A Review of Literature Data. *J Clin Med*, *5*(8). https://doi.org/10.3390/jcm5080067

Budi, E. H., Schaub, J. R., Decaris, M., Turner, S., & Derynck, R. (2021). TGF-beta as a driver of fibrosis: physiological roles and therapeutic opportunities. *J Pathol*, *254*(4), 358-373. https://doi.org/10.1002/path.5680

Chan, H. Y., Chang, C. J., Chiang, S. C., Chen, J. J., Chen, C. H., Sun, H. J., Hwu, H. G., & Lai, M. S. (2010). A randomised controlled study of risperidone and olanzapine for schizophrenic patients with neuroleptic-induced acute dystonia or parkinsonism. *J Psychopharmacol*, *24*(1), 91-98. https://doi.org/10.1177/0269881108096070

Chandrasekaran, K., Mehrabian, Z., Spinnewyn, B., Drieu, K., & Fiskum, G. (2001). Neuroprotective effects of bilobalide, a component of the Ginkgo biloba extract (EGb 761), in gerbil global brain ischemia. *Brain Res*, *922*(2), 282-292. https://doi.org/10.1016/s0006-8993(01)03188-2

Chang, L. (2011). The role of stress on physiologic responses and clinical symptoms in irritable bowel syndrome. *Gastroenterology*, *140*(3), 761-765. https://doi.org/10.1053/j.gastro.2011.01.032

Chen, L., Deng, H., Cui, H., Fang, J., Zuo, Z., Deng, J., Li, Y., Wang, X., & Zhao, L. (2018). Inflammatory responses and inflammation-associated diseases in organs. *Oncotarget*, *9*(6), 7204-7218. https://doi.org/10.18632/oncotarget.23208

Chopra, B., & Dhingra, A. K. (2021). Natural products: A lead for drug discovery and development. *Phytother Res*, *35*(9), 4660-4702. https://doi.org/10.1002/ptr.7099

Cooper, T. E., Khalid, R., Chan, S., Craig, J. C., Hawley, C. M., Howell, M., Johnson, D. W., Jaure, A., Teixeira-Pinto, A., & Wong, G. (2023). Synbiotics, prebiotics and probiotics for people with chronic kidney disease. *Cochrane Database Syst Rev*, *10*(10), CD013631. https://doi.org/10.1002/14651858.CD013631.pub2

Cortez-Navarrete, M., Perez-Rubio, K. G., & Escobedo-Gutierrez, M. J. (2023). Role of Fenugreek, Cinnamon, Curcuma longa, Berberine and Momordica charantia in Type 2 Diabetes Mellitus Treatment: A Review. *Pharmaceuticals (Basel)*, *16*(4). https://doi.org/10.3390/ph16040515

da Fonseca, L. R., Rodrigues, R. A., Ramos, A. S., da Cruz, J. D., Ferreira, J. L. P., Silva, J. R. A., & Amaral, A. C. F. (2020). Herbal Medicinal Products from Passiflora for Anxiety: An Unexploited Potential. *ScientificWorldJournal*, *2020*, 6598434. https://doi.org/10.1155/2020/6598434

Dai, C., Lin, J., Li, H., Shen, Z., Wang, Y., Velkov, T., & Shen, J. (2022). The Natural Product Curcumin as an Antibacterial Agent: Current Achievements and Problems. *Antioxidants (Basel)*, *11*(3). https://doi.org/10.3390/antiox11030459

Darbandi, A., Asadi, A., Ghanavati, R., Afifirad, R., Emamie, A. D., Kakanj, M., & Talebi, M. (2021). Corrigendum to 'The effect of probiotics on respiratory tract infection with special emphasis on COVID-19: Systemic review 2010-20' [International Journal of Infectious Diseases 105 (April 2021) 91-104]. *Int J Infect Dis*, *110*, 337. https://doi.org/10.1016/j.ijid.2021.08.002

Dean, O., Giorlando, F., & Berk, M. (2011). N-acetylcysteine in psychiatry: current therapeutic evidence and potential mechanisms of action. *J Psychiatry Neurosci*, *36*(2), 78-86. https://doi.org/10.1503/jpn.100057

Declercq, J., De Leeuw, E., & Lambrecht, B. N. (2022). Inflammasomes and IL-1 family cytokines in SARS-CoV-2 infection: from prognostic marker to therapeutic agent. *Cytokine*, *157*, 155934. https://doi.org/10.1016/j.cyto.2022.155934

Desbonnet, L., Garrett, L., Clarke, G., Bienenstock, J., & Dinan, T. G. (2008). The probiotic Bifidobacteria infantis: An assessment of potential antidepressant properties in the rat. *J Psychiatr Res*, *43*(2), 164-174. https://doi.org/10.1016/j.jpsychires.2008.03.009

Dias, D. A., Urban, S., & Roessner, U. (2012). A historical overview of natural products in drug discovery. *Metabolites*, *2*(2), 303-336. https://doi.org/10.3390/metabo2020303

Diaz-Gonzalez, F., & Hernandez-Hernandez, M. V. (2023). Rheumatoid arthritis. *Med Clin*

(Barc), *161*(12), 533-542. https://doi.org/10.1016/j.medcli.2023.07.014 (Artritis reumatoide.)

Dicks, L. M. T. (2022). Gut Bacteria and Neurotransmitters. *Microorganisms*, *10*(9). https://doi.org/10.3390/microorganisms10091838

Dicks, L. M. T., Hurn, D., & Hermanus, D. (2021). Gut Bacteria and Neuropsychiatric Disorders. *Microorganisms*, *9*(12). https://doi.org/10.3390/microorganisms9122583

Dorhoi, A., & Kaufmann, S. H. (2014). Tumor necrosis factor alpha in mycobacterial infection. *Semin Immunol*, *26*(3), 203-209. https://doi.org/10.1016/j.smim.2014.04.003

Doruk, A., Uzun, O., & Ozsahin, A. (2008). A placebo-controlled study of extract of ginkgo biloba added to clozapine in patients with treatment-resistant schizophrenia. *Int Clin Psychopharmacol*, *23*(4), 223-227. https://doi.org/10.1097/YIC.0b013e3282fcff2f

Elenkov, I. J., Wilder, R. L., Chrousos, G. P., & Vizi, E. S. (2000). The sympathetic nerve--an integrative interface between two supersystems: the brain and the immune system. *Pharmacol Rev*, *52*(4), 595-638. https://www.ncbi.nlm.nih.gov/pubmed/11121511

El-Saadony, M. T., Yang, T., Korma, S. A., Sitohy, M., Abd El-Mageed, T. A., Selim, S., Al Jaouni, S. K., Salem, H. M., Mahmmod, Y., Soliman, S. M., Mo'men, S. A. A., Mosa, W. F. A., El-Wafai, N. A., Abou-Aly, H. E., Sitohy, B., Abd El-Hack, M. E., El-Tarabily, K. A., & Saad, A. M. (2022). Impacts of turmeric and its principal bioactive curcumin on human health: Pharmaceutical, medicinal, and food applications: A comprehensive review. *Front Nutr*, *9*, 1040259. https://doi.org/10.3389/fnut.2022.1040259

Ergen, E. N., & Yusuf, N. (2018). Inhibition of interleukin-12 and/or interleukin-23 for the treatment of psoriasis: What is the evidence for an effect on malignancy? *Exp Dermatol*, *27*(7), 737-747. https://doi.org/10.1111/exd.13676

Ewaschuk, J. B., & Dieleman, L. A. (2006). Probiotics and prebiotics in chronic inflammatory bowel diseases. *World J Gastroenterol*, *12*(37), 5941-5950. https://doi.org/10.3748/wjg.v12.i37.5941

Florio, R., De Filippis, B., Veschi, S., di Giacomo, V., Lanuti, P., Catitti, G., Brocco, D., di Rienzo, A., Cataldi, A., Cacciatore, I., Amoroso, R., Cama, A., & De Lellis, L. (2023). Resveratrol Derivative Exhibits Marked Antiproliferative Actions, Affecting Stemness in Pancreatic Cancer Cells. *Int J Mol Sci*, *24*(3). https://doi.org/10.3390/ijms24031977

Foo, J., Bellot, G., Pervaiz, S., & Alonso, S. (2022). Mitochondria-mediated oxidative stress during viral infection. *Trends Microbiol*, *30*(7), 679-692. https://doi.org/10.1016/j.tim.2021.12.011

Fu, J., & Wu, H. (2023). Structural Mechanisms of NLRP3 Inflammasome Assembly and Activation. *Annu Rev Immunol*, *41*, 301-316. https://doi.org/10.1146/annurev-immunol-081022-021207

Gazdag, G., Szabo, Z., & Szlavik, J. (2014). [Psychiatric aspects of infectious diseases -- a literature review]. *Neuropsychopharmacol Hung*, *16*(4), 181-187. https://www.ncbi.nlm.nih.gov/pubmed/25577481 (A fertozo betegsegek pszichiatriai vonatkozasai -- irodalmi attekintes.)

Georgescu, A. M., Banescu, C., Azamfirei, R., Hutanu, A., Moldovan, V., Badea, I., Voidazan, S., Dobreanu, M., Chirtes, I. R., & Azamfirei, L. (2020). Evaluation of TNF-alpha genetic polymorphisms as predictors for sepsis susceptibility and progression. *BMC Infect Dis*, *20*(1), 221. https://doi.org/10.1186/s12879-020-4910-6

Goldberg, R. J., & Katz, J. (2007). A meta-analysis of the analgesic effects of omega-3 polyunsaturated fatty acid supplementation for inflammatory joint pain. *Pain*, *129*(1-2), 210-223. https://doi.org/10.1016/j.pain.2007.01.020

Goldman, R. D. (2014). Honey for treatment of cough in children. *Can Fam Physician*, *60*(12), 1107-1108, 1110. https://www.ncbi.nlm.nih.gov/pubmed/25642485

Gow, R. V., & Hibbeln, J. R. (2014). Omega-3 fatty acid and nutrient deficits in adverse neurodevelopment and childhood behaviors. *Child Adolesc Psychiatr Clin N Am*, *23*(3), 555-590. https://doi.org/10.1016/j.chc.2014.02.002

Grasshoff, H., Comduhr, S., Monne, L. R., Muller, A., Lamprecht, P., Riemekasten, G., & Humrich, J. Y. (2021). Low-Dose IL-2 Therapy in Autoimmune and Rheumatic Diseases. *Front Immunol*, *12*, 648408. https://doi.org/10.3389/fimmu.2021.648408

Grassi, D., Desideri, G., & Ferri, C. (2010). Flavonoids: antioxidants against atherosclerosis. *Nutrients*, *2*(8), 889-902. https://doi.org/10.3390/nu2080889

Han, P. P., Han, Y., Shen, X. Y., Gao, Z. K., & Bi, X. (2023). NLRP3 inflammasome activation after ischemic stroke. *Behav Brain Res*, *452*, 114578. https://doi.org/10.1016/j.bbr.2023.114578

Haruwaka, K., Ikegami, A., Tachibana, Y., Ohno, N., Konishi, H., Hashimoto, A., Matsumoto, M., Kato, D., Ono, R., Kiyama, H., Moorhouse, A. J., Nabekura, J., & Wake, H. (2019). Dual microglia effects on blood brain barrier permeability induced by systemic inflammation. *Nat Commun*, *10*(1), 5816. https://doi.org/10.1038/s41467-019-13812-z

He, Y., Yue, Y., Zheng, X., Zhang, K., Chen, S., & Du, Z. (2015). Curcumin, inflammation, and chronic diseases: how are they linked? *Molecules*, *20*(5), 9183-9213. https://doi.org/10.3390/molecules200591883

Henderson, C., & Goldbach-Mansky, R. (2010). Monogenic IL-1 mediated autoinflammatory and immunodeficiency syndromes: finding the right balance in response to danger signals. *Clin Immunol*, *135*(2), 210-222. https://doi.org/10.1016/j.clim.2010.02.013

Herder, C., Dalmas, E., Boni-Schnetzler, M., & Donath, M. Y. (2015). The IL-1 Pathway in Type 2 Diabetes and Cardiovascular Complications. *Trends Endocrinol Metab*, *26*(10), 551-563. https://doi.org/10.1016/j.tem.2015.08.001

Hewagalamulage, S. D., Lee, T. K., Clarke, I. J., & Henry, B. A. (2016). Stress, cortisol, and obesity: a role for cortisol responsiveness in identifying individuals prone to obesity. *Domest Anim Endocrinol*, *56 Suppl*, S112-120. https://doi.org/10.1016/j.domaniend.2016.03.004

Hewlings, S. J., & Kalman, D. S. (2017). Curcumin: A Review of Its Effects on Human Health. *Foods*, *6*(10). https://doi.org/10.3390/foods6100092

Hocaoglu, A. B., Karaman, O., Erge, D. O., Erbil, G., Yilmaz, O., Bagriyanik, A., & Uzuner, N. (2011). Glycyrrhizin and long-term histopathologic changes in a murine model of asthma. *Curr Ther Res Clin Exp*, *72*(6), 250-261. https://doi.org/10.1016/j.curtheres.2011.11.002

Hoenders, H. J. R., Bartels-Velthuis, A. A., Vollbehr, N. K., Bruggeman, R., Knegtering, H., & de Jong, J. (2018). Natural Medicines for Psychotic Disorders: A Systematic Review. *J Nerv Ment Dis*, *206*(2), 81-101. https://doi.org/10.1097/NMD.0000000000000782

Hoffer, L. J. (2008). Vitamin therapy in schizophrenia. *Isr J Psychiatry Relat Sci*, *45*(1), 3-10. https://www.ncbi.nlm.nih.gov/pubmed/18587164

Hope, S., Ueland, T., Steen, N. E., Dieset, I., Lorentzen, S., Berg, A. O., Agartz, I., Aukrust, P., & Andreassen, O. A. (2013). Interleukin 1 receptor antagonist and soluble tumor necrosis factor receptor 1 are associated with general severity and psychotic symptoms in schizophrenia and bipolar disorder. *Schizophr Res*, *145*(1-3), 36-42. https://doi.org/10.1016/j.schres.2012.12.023

Hourani, T., Sharma, A., Luwor, R. B., & Achuthan, A. A. (2024). Transforming growth factor-beta in tumor microenvironment: Understanding its impact on monocytes and macrophages for its targeting. *Int Rev Immunol*, 1-16. https://doi.org/10.1080/08830185.2024.2411998

Hsu, M. C., Huang, Y. S., & Ouyang, W. C. (2020). Beneficial effects of omega-3 fatty acid supplementation in schizophrenia: possible mechanisms. *Lipids Health Dis*, *19*(1), 159. https://doi.org/10.1186/s12944-020-01337-0

Huang, Y., Zhang, X., & Zhou, N. (2022). The Interrelation between Interleukin-2 and Schizophrenia. *Brain Sci*, *12*(9). https://doi.org/10.3390/brainsci12091154

Hussain, Y., Alam, W., Ullah, H., Dacrema, M., Daglia, M., Khan, H., & Arciola, C. R. (2022). Antimicrobial Potential of Curcumin: Therapeutic Potential and Challenges to Clinical Applications. *Antibiotics (Basel)*, *11*(3). https://doi.org/10.3390/antibiotics11030322

Idriss, H. T., & Naismith, J. H. (2000). TNF alpha and the TNF receptor superfamily: structure-function relationship(s). *Microsc Res Tech*, *50*(3), 184-195. https://doi.org/10.1002/1097-

0029(20000801)50:3<184::AID-JEMT2>3.0.CO;2-H

Janda, K., Wojtkowska, K., Jakubczyk, K., Antoniewicz, J., & Skonieczna-Zydecka, K. (2020). Passiflora incarnata in Neuropsychiatric Disorders-A Systematic Review. *Nutrients*, *12*(12). https://doi.org/10.3390/nu12123894

Jang, D. I., Lee, A. H., Shin, H. Y., Song, H. R., Park, J. H., Kang, T. B., Lee, S. R., & Yang, S. H. (2021). The Role of Tumor Necrosis Factor Alpha (TNF-alpha) in Autoimmune Disease and Current TNF-alpha Inhibitors in Therapeutics. *Int J Mol Sci*, *22*(5). https://doi.org/10.3390/ijms22052719

Jang, J. Y., Im, E., & Kim, N. D. (2022). Mechanism of Resveratrol-Induced Programmed Cell Death and New Drug Discovery against Cancer: A Review. *Int J Mol Sci*, *23*(22). https://doi.org/10.3390/ijms232213689

Jomova, K., Raptova, R., Alomar, S. Y., Alwasel, S. H., Nepovimova, E., Kuca, K., & Valko, M. (2023). Reactive oxygen species, toxicity, oxidative stress, and antioxidants: chronic diseases and aging. *Arch Toxicol*, *97*(10), 2499-2574. https://doi.org/10.1007/s00204-023-03562-9

Jugran, A. K., Rawat, S., Devkota, H. P., Bhatt, I. D., & Rawal, R. S. (2021). Diabetes and plant-derived natural products: From ethnopharmacological approaches to their potential for modern drug discovery and development. *Phytother Res*, *35*(1), 223-245. https://doi.org/10.1002/ptr.6821

Kale, A., Naphade, N., Sapkale, S., Kamaraju, M., Pillai, A., Joshi, S., & Mahadik, S. (2010). Reduced folic acid, vitamin B12 and docosahexaenoic acid and increased homocysteine and cortisol in never-medicated schizophrenia patients: implications for altered one-carbon metabolism. *Psychiatry Res*, *175*(1-2), 47-53. https://doi.org/10.1016/j.psychres.2009.01.013

Karabekir, S. C., & Ozgorgulu, A. (2020). Possible protective effects of resveratrol in hepatocellular carcinoma. *Iran J Basic Med Sci*, *23*(1), 71-78. https://doi.org/10.22038/IJBMS.2019.36821.8774

Khare, T., Anand, U., Dey, A., Assaraf, Y. G., Chen, Z. S., Liu, Z., & Kumar, V. (2021). Exploring Phytochemicals for Combating Antibiotic Resistance in Microbial Pathogens. *Front Pharmacol*, *12*, 720726. https://doi.org/10.3389/fphar.2021.720726

Kim, J. H., Jin, H. M., Kim, K., Song, I., Youn, B. U., Matsuo, K., & Kim, N. (2009). The mechanism of osteoclast differentiation induced by IL-1. *J Immunol*, *183*(3), 1862-1870. https://doi.org/10.4049/jimmunol.0803007

Kim, S. K., Guevarra, R. B., Kim, Y. T., Kwon, J., Kim, H., Cho, J. H., Kim, H. B., & Lee, J. H. (2019). Role of Probiotics in Human Gut Microbiome-Associated Diseases. *J Microbiol Biotechnol*, *29*(9), 1335-1340. https://doi.org/10.4014/jmb.1906.06064

Kolliker-Frers, R., Udovin, L., Otero-Losada, M., Kobiec, T., Herrera, M. I., Palacios, J., Razzitte, G., & Capani, F. (2021). Neuroinflammation: An Integrating Overview of Reactive-Neuroimmune Cell Interactions in Health and Disease. *Mediators Inflamm*, *2021*, 9999146. https://doi.org/10.1155/2021/9999146

Kroth, A., Santos, M., Borella da Silva, T. C., Santos Silveira, E. M., & Partata, W. A. (2021). Aqueous leaf extract from Luehea divaricata Mart. Modulates oxidative stress markers in the spinal cord of rats with neuropathic pain. *J Ethnopharmacol*, *268*, 113674. https://doi.org/10.1016/j.jep.2020.113674

Kuke C, Williamson EM, Roberts MF, Lajubutu BA, et al 1998. Anti-inflamatory activity of bi-naphthoquinones from *Diospyros* sp. Phytotherapy Research. 12 :155-158. https://doi.org/10.1002/(SICI)1099-1573(199805)12:3<155::AID-PTR214>3.0.CO;2-1

Kulamarva, K., Shivakumar, V., Chikkanna, U., Ramakrishna, K. K., Bhargav, H., & Varambally, S. (2023). Role of Ayurveda in the management of psychotic disorders: A systematic review of clinical evidence. *J Ayurveda Integr Med*, *14*(3), 100720. https://doi.org/10.1016/j.jaim.2023.100720

Lane, H. Y., Liu, Y. C., Huang, C. L., Chang, Y. C., Liau, C. H., Perng, C. H., & Tsai, G. E. (2008). Sarcosine (N-methylglycine) treatment for acute schizophrenia: a randomized, double-blind study. *Biol Psychiatry*, *63*(1), 9-12. https://doi.org/10.1016/j.biopsych.2007.04.038

Lanka, S., K, V. R., Arji, A., Raju, R., Suvvari, T. K., Thakwani, M., Laxmi Supriya, Y., Meenavilli, B. C., Ravuru, S. K., & Sivaraj, N. (2024). Association of Tumor Necrosis

Factor-Alpha (TNF-alpha) rs1800629 Polymorphism in Chronic Kidney Disease. *Cureus*, *16*(5), e60332. https://doi.org/10.7759/cureus.60332

Levast, B., Li, Z., & Madrenas, J. (2015). The role of IL-10 in microbiome-associated immune modulation and disease tolerance. *Cytokine*, *75*(2), 291-301. https://doi.org/10.1016/j.cyto.2014.11.027

Li, J., Xu, P., Hong, Y., Xie, Y., Peng, M., Sun, R., Guo, H., Zhang, X., Zhu, W., Wang, J., & Liu, X. (2023). Lipocalin-2-mediated astrocyte pyroptosis promotes neuroinflammatory injury via NLRP3 inflammasome activation in cerebral ischemia/reperfusion injury. *J Neuroinflammation*, *20*(1), 148. https://doi.org/10.1186/s12974-023-02819-5

Li, M. O., Wan, Y. Y., Sanjabi, S., Robertson, A. K., & Flavell, R. A. (2006). Transforming growth factor-beta regulation of immune responses. *Annu Rev Immunol*, *24*, 99-146. https://doi.org/10.1146/annurev.immunol.24.021605.090737

Li, S. J., Perez-Chada, L. M., & Merola, J. F. (2019). TNF Inhibitor-Induced Psoriasis: Proposed Algorithm for Treatment and Management. *J Psoriasis Psoriatic Arthritis*, *4*(2), 70-80. https://doi.org/10.1177/2475530318810851

Li, X., Wang, Q., Hu, X., & Liu, W. (2022). Current Status of Probiotics as Supplements in the Prevention and Treatment of Infectious Diseases. *Front Cell Infect Microbiol*, *12*, 789063. https://doi.org/10.3389/fcimb.2022.789063

Liu, Q., Zhang, D., Hu, D., Zhou, X., & Zhou, Y. (2018). The role of mitochondria in NLRP3 inflammasome activation. *Mol Immunol*, *103*, 115-124. https://doi.org/10.1016/j.molimm.2018.09.010

Ly, M., Yu, G. Z., Mian, A., Cramer, A., Meysami, S., Merrill, D. A., Samara, A., Eisenstein, S. A., Hershey, T., Babulal, G. M., Lenze, E. J., Morris, J. C., Benzinger, T. L. S., & Raji, C. A. (2023). Neuroinflammation: A Modifiable Pathway Linking Obesity, Alzheimer's disease, and Depression. *Am J Geriatr Psychiatry*, *31*(10), 853-866. https://doi.org/10.1016/j.jagp.2023.06.001

Mannino, M. H., Zhu, Z., Xiao, H., Bai, Q., Wakefield, M. R., & Fang, Y. (2015). The paradoxical role of IL-10 in immunity and cancer. *Cancer Lett*, *367*(2), 103-107. https://doi.org/10.1016/j.canlet.2015.07.009

Mapunda, J. A., Tibar, H., Regragui, W., & Engelhardt, B. (2022). How Does the Immune System Enter the Brain? *Front Immunol*, *13*, 805657. https://doi.org/10.3389/fimmu.2022.805657

Mayer, M. G., & Fischer, T. (2024). Microglia at the blood brain barrier in health and disease. *Front Cell Neurosci*, *18*, 1360195. https://doi.org/10.3389/fncel.2024.1360195

McEwen, B. S. (2007). Physiology and neurobiology of stress and adaptation: central role of the brain. *Physiol Rev*, *87*(3), 873-904. https://doi.org/10.1152/physrev.00041.2006

Michalicova, A., Majerova, P., & Kovac, A. (2020). Tau Protein and Its Role in Blood-Brain Barrier Dysfunction. *Front Mol Neurosci*, *13*, 570045. https://doi.org/10.3389/fnmol.2020.570045

Mikulska, J., Juszczyk, G., Gawronska-Grzywacz, M., & Herbet, M. (2021). HPA Axis in the Pathomechanism of Depression and Schizophrenia: New Therapeutic Strategies Based on Its Participation. *Brain Sci*, *11*(10). https://doi.org/10.3390/brainsci11101298

Miller, A. H., & Raison, C. L. (2016). The role of inflammation in depression: from evolutionary imperative to modern treatment target. *Nat Rev Immunol*, *16*(1), 22-34. https://doi.org/10.1038/nri.2015.5

Millett, C. E., Harder, J., Locascio, J. J., Shanahan, M., Santone, G., Fichorova, R. N., Corrigan, A., Baecher-Allan, C., & Burdick, K. E. (2020). TNF-alpha and its soluble receptors mediate the relationship between prior severe mood episodes and cognitive dysfunction in euthymic bipolar disorder. *Brain Behav Immun*, *88*, 403-410. https://doi.org/10.1016/j.bbi.2020.04.003

Mizui, M. (2019). Natural and modified IL-2 for the treatment of cancer and autoimmune diseases. *Clin Immunol*, *206*, 63-70. https://doi.org/10.1016/j.clim.2018.11.002

Moore, K. W., de Waal Malefyt, R., Coffman, R. L., & O'Garra, A. (2001). Interleukin-10 and the interleukin-10 receptor. *Annu Rev Immunol*, *19*, 683-765. https://doi.org/10.1146/annurev.immunol.19.1.683

Moorman, C. D., Sohn, S. J., & Phee, H. (2021). Emerging Therapeutics for Immune Tolerance: Tolerogenic Vaccines, T cell Therapy, and IL-2 Therapy. *Front Immunol*,

12, 657768. https://doi.org/10.3389/fimmu.2021.657768

Mou, Y., Du, Y., Zhou, L., Yue, J., Hu, X., Liu, Y., Chen, S., Lin, X., Zhang, G., Xiao, H., & Dong, B. (2022). Gut Microbiota Interact With the Brain Through Systemic Chronic Inflammation: Implications on Neuroinflammation, Neurodegeneration, and Aging. *Front Immunol*, *13*, 796288. https://doi.org/10.3389/fimmu.2022.796288

Munjal, S., Ferrando, S. J., & Freyberg, Z. (2017). Neuropsychiatric Aspects of Infectious Diseases: An Update. *Crit Care Clin*, *33*(3), 681-712. https://doi.org/10.1016/j.ccc.2017.03.007

Murakami, T., Takahata, Y., Hata, K., & Nishimura, R. (2020). Role of interleukin-1 and inflammasomes in oral disease. *J Oral Biosci*, *62*(3), 242-248. https://doi.org/10.1016/j.job.2020.07.003

Murphy, F., Nasa, A., Cullinane, D., Raajakesary, K., Gazzaz, A., Sooknarine, V., Haines, M., Roman, E., Kelly, L., O'Neill, A., Cannon, M., & Roddy, D. W. (2022). Childhood Trauma, the HPA Axis and Psychiatric Illnesses: A Targeted Literature Synthesis. *Front Psychiatry*, *13*, 748372. https://doi.org/10.3389/fpsyt.2022.748372

Novelli, F., & Casanova, J. L. (2004). The role of IL-12, IL-23 and IFN-gamma in immunity to viruses. *Cytokine Growth Factor Rev*, *15*(5), 367-377. https://doi.org/10.1016/j.cytogfr.2004.03.009

O'Connor, D. B., Gartland, N., & O'Connor, R. C. (2020). Stress, cortisol and suicide risk. *Int Rev Neurobiol*, *152*, 101-130. https://doi.org/10.1016/bs.irn.2019.11.006

Omidkhoda, S. F., & Hosseinzadeh, H. (2022). Saffron and its active ingredients against human disorders: A literature review on existing clinical evidence. *Iran J Basic Med Sci*, *25*(8), 913-933. https://doi.org/10.22038/IJBMS.2022.63378.13985

Orange, S. T., Leslie, J., Ross, M., Mann, D. A., & Wackerhage, H. (2023). The exercise IL-6 enigma in cancer. *Trends Endocrinol Metab*, *34*(11), 749-763. https://doi.org/10.1016/j.tem.2023.08.001

Ortiz, G. G., Pacheco-Moises, F. P., Macias-Islas, M. A., Flores-Alvarado, L. J., Mireles-Ramirez, M. A., Gonzalez-Renovato, E. D., Hernandez-Navarro, V. E., Sanchez-Lopez, A. L., & Alatorre-Jimenez, M. A. (2014). Role of the blood-brain barrier in multiple sclerosis. *Arch Med Res*, *45*(8), 687-697. https://doi.org/10.1016/j.arcmed.2014.11.013

Othman, L., Sleiman, A., & Abdel-Massih, R. M. (2019). Antimicrobial Activity of Polyphenols and Alkaloids in Middle Eastern Plants. *Front Microbiol*, *10*, 911. https://doi.org/10.3389/fmicb.2019.00911

Pandolfi, F., Franza, L., Carusi, V., Altamura, S., Andriollo, G., & Nucera, E. (2020). Interleukin-6 in Rheumatoid Arthritis. *Int J Mol Sci*, *21*(15). https://doi.org/10.3390/ijms21155238

Papadimitriou, A., & Priftis, K. N. (2009). Regulation of the hypothalamic-pituitary-adrenal axis. *Neuroimmunomodulation*, *16*(5), 265-271. https://doi.org/10.1159/000216184

Patlola, S. R., Donohoe, G., & McKernan, D. P. (2023). The relationship between inflammatory biomarkers and cognitive dysfunction in patients with schizophrenia: A systematic review and meta-analysis. *Prog Neuropsychopharmacol Biol Psychiatry*, *121*, 110668. https://doi.org/10.1016/j.pnpbp.2022.110668

Pfingstgraf, I. O., Taulescu, M., Pop, R. M., Orasan, R., Vlase, L., Uifalean, A., Todea, D., Alexescu, T., Toma, C., & Parvu, A. E. (2021). Protective Effects of Taraxacum officinale L. (Dandelion) Root Extract in Experimental Acute on Chronic Liver Failure. *Antioxidants (Basel)*, *10*(4). https://doi.org/10.3390/antiox10040504

Poladian, N., Orujyan, D., Narinyan, W., Oganyan, A. K., Navasardyan, I., Velpuri, P., Chorbajian, A., & Venketaraman, V. (2023). Role of NF-kappaB during Mycobacterium tuberculosis Infection. *Int J Mol Sci*, *24*(2). https://doi.org/10.3390/ijms24021772

Puri, V., Nagpal, M., Singh, I., Singh, M., Dhingra, G. A., Huanbutta, K., Dheer, D., Sharma, A., & Sangnim, T. (2022). A Comprehensive Review on Nutraceuticals: Therapy Support and Formulation Challenges. *Nutrients*, *14*(21). https://doi.org/10.3390/nu14214637

Qu, D., Liu, J., Lau, C. W., & Huang, Y. (2014). IL-6 in diabetes and cardiovascular complications. *Br J Pharmacol*, *171*(15), 3595-3603. https://doi.org/10.1111/bph.12713

Ralph, B. A., Lehoux, M., Ostapska, H., Snarr, B. D., Caffrey-Carr, A. K., Fraser, R., Saleh, M., Obar, J. J., Qureshi, S. T., & Sheppard,

D. C. (2021). The IL-1 Receptor Is Required to Maintain Neutrophil Viability and Function During Aspergillus fumigatus Airway Infection. *Front Immunol*, *12*, 675294. https://doi.org/10.3389/fimmu.2021.675294

Rees, A., Dodd, G. F., & Spencer, J. P. E. (2018). The Effects of Flavonoids on Cardiovascular Health: A Review of Human Intervention Trials and Implications for Cerebrovascular Function. *Nutrients*, *10*(12). https://doi.org/10.3390/nu10121852

Ridker, P. M., & Rane, M. (2021). Interleukin-6 Signaling and Anti-Interleukin-6 Therapeutics in Cardiovascular Disease. *Circ Res*, *128*(11), 1728-1746. https://doi.org/10.1161/CIRCRESAHA.121.319077

Ried, K. (2020). Garlic lowers blood pressure in hypertensive subjects, improves arterial stiffness and gut microbiota: A review and meta-analysis. *Exp Ther Med*, *19*(2), 1472-1478. https://doi.org/10.3892/etm.2019.8374

Rios, J. L., Francini, F., & Schinella, G. R. (2015). Natural Products for the Treatment of Type 2 Diabetes Mellitus. *Planta Med*, *81*(12-13), 975-994. https://doi.org/10.1055/s-0035-1546131

Roberts, J. D., Willmott, A. G. B., Beasley, L., Boal, M., Davies, R., Martin, L., Chichger, H., Gautam, L., & Del Coso, J. (2021). The Impact of Decaffeinated Green Tea Extract on Fat Oxidation, Body Composition and Cardio-Metabolic Health in Overweight, Recreationally Active Individuals. *Nutrients*, *13*(3). https://doi.org/10.3390/nu13030764

Rose-John, S. (2021). Blocking only the bad side of IL-6 in inflammation and cancer. *Cytokine*, *148*, 155690. https://doi.org/10.1016/j.cyto.2021.155690

Ruscitti, P., Cipriani, P., Liakouli, V., Carubbi, F., Berardicurti, O., Di Benedetto, P., Ciccia, F., Guggino, G., Alvaro, S., Triolo, G., & Giacomelli, R. (2018). The Emerging Role of IL-1 Inhibition in Patients Affected by Rheumatoid Arthritis and Diabetes. *Rev Recent Clin Trials*, *13*(3), 210-214. https://doi.org/10.2174/1574887113666180314102651

Ruze, R., Liu, T., Zou, X., Song, J., Chen, Y., Xu, R., Yin, X., & Xu, Q. (2023). Obesity and type 2 diabetes mellitus: connections in epidemiology, pathogenesis, and treatments. *Front Endocrinol (Lausanne)*, *14*, 1161521. https://doi.org/10.3389/fendo.2023.1161521

Sadowska, A. M., Verbraecken, J., Darquennes, K., & De Backer, W. A. (2006). Role of N-acetylcysteine in the management of COPD. *Int J Chron Obstruct Pulmon Dis*, *1*(4), 425-434. https://doi.org/10.2147/copd.2006.1.4.425

Sahin, K., Gencoglu, H., Korkusuz, A. K., Orhan, C., Aldatmaz, I. E., Erten, F., Er, B., Morde, A., Padigaru, M., & Kilic, E. (2024). Impact of a Novel Valerian Extract on Sleep Quality, Relaxation, and GABA/Serotonin Receptor Activity in a Murine Model. *Antioxidants (Basel)*, *13*(6). https://doi.org/10.3390/antiox13060657

Saleem, A., Qurat Ul, A., & Akhtar, M. F. (2022). Alternative Therapy of Psychosis: Potential Phytochemicals and Drug Targets in the Management of Schizophrenia. *Front Pharmacol*, *13*, 895668. https://doi.org/10.3389/fphar.2022.895668

Sanmarco, L. M., Polonio, C. M., Wheeler, M. A., & Quintana, F. J. (2021). Functional immune cell-astrocyte interactions. *J Exp Med*, *218*(9). https://doi.org/10.1084/jem.20202715

Sarmin, N., Roknuzzaman, A. S. M., Sarker, R., Or-Rashid, M., Qusar, M. S., Bachar, S. C., Kabir, E. R., Islam, M. R., & Al Mahmud, Z. (2024). Association of interleukin-2 and interleukin-10 with the pathophysiology and development of generalized anxiety disorder: a case-control study. *BMC Psychiatry*, *24*(1), 462. https://doi.org/10.1186/s12888-024-05911-z

Shafiee, M., Arekhi, S., Omranzadeh, A., & Sahebkar, A. (2018). Saffron in the treatment of depression, anxiety and other mental disorders: Current evidence and potential mechanisms of action. *J Affect Disord*, *227*, 330-337. https://doi.org/10.1016/j.jad.2017.11.020

Shearer, G. C., Savinova, O. V., & Harris, W. S. (2012). Fish oil -- how does it reduce plasma triglycerides? *Biochim Biophys Acta*, *1821*(5), 843-851. https://doi.org/10.1016/j.bbalip.2011.10.011

Shen, X., Ma, C., Yang, Y., Liu, X., Wang, B., Wang, Y., Zhang, G., Bian, X., & Zhang, N. (2024). The Role and Mechanism of Probiotics Supplementation in Blood Glucose Regulation: A Review. *Foods*, *13*(17). https://doi.org/10.3390/foods13172719

Shibuya, M., Watanabe, Y., Nunokawa, A., Egawa, J., Kaneko, N., Igeta, H., & Someya, T. (2014). Interleukin 1 beta gene and risk of schizophrenia: detailed case-control and family-based studies and an updated meta-analysis. *Hum Psychopharmacol*, *29*(1), 31-37. https://doi.org/10.1002/hup.2365

Siddiqui, M. Z. (2011). Boswellia serrata, a potential antiinflammatory agent: an overview. *Indian J Pharm Sci*, *73*(3), 255-261. https://doi.org/10.4103/0250-474X.93507

Singh, B. N., Shankar, S., & Srivastava, R. K. (2011). Green tea catechin, epigallocatechin-3-gallate (EGCG): mechanisms, perspectives and clinical applications. *Biochem Pharmacol*, *82*(12), 1807-1821. https://doi.org/10.1016/j.bcp.2011.07.093

Singh, R. K., Chang, H. W., Yan, D., Lee, K. M., Ucmak, D., Wong, K., Abrouk, M., Farahnik, B., Nakamura, M., Zhu, T. H., Bhutani, T., & Liao, W. (2017). Influence of diet on the gut microbiome and implications for human health. *J Transl Med*, *15*(1), 73. https://doi.org/10.1186/s12967-017-1175-y

Singh, V., Singh, S. P., & Chan, K. (2010). Review and meta-analysis of usage of ginkgo as an adjunct therapy in chronic schizophrenia. *Int J Neuropsychopharmacol*, *13*(2), 257-271. https://doi.org/10.1017/S1461145709990654

Spanoudaki, M., Papadopoulou, S. K., Antasouras, G., Papadopoulos, K. A., Psara, E., Vorvolakos, T., Solovos, E., Chrysafi, M., Psallas, M., Mentzelou, M., Ourda, D., & Giaginis, C. (2024). Curcumin as a Multifunctional Spice Ingredient against Mental Disorders in Humans: Current Clinical Studies and Bioavailability Concerns. *Life (Basel)*, *14*(4). https://doi.org/10.3390/life14040479

Sukhareva, E. V. (2021). The role of the corticotropin-releasing hormone and its receptors in the regulation of stress response. *Vavilovskii Zhurnal Genet Selektsii*, *25*(2), 216-223. https://doi.org/10.18699/VJ21.025

Szymczak, J., Grygiel-Gorniak, B., & Cielecka-Piontek, J. (2024). Zingiber Officinale Roscoe: The Antiarthritic Potential of a Popular Spice-Preclinical and Clinical Evidence. *Nutrients*, *16*(5). https://doi.org/10.3390/nu16050741

Tammadon, M. R., Nobahar, M., Hydarinia-Naieni, Z., Ebrahimian, A., Ghorbani, R., & Vafaei, A. A. (2021). The Effects of Valerian on Sleep Quality, Depression, and State Anxiety in Hemodialysis Patients: A Randomized, Double-blind, Crossover Clinical Trial. *Oman Med J*, *36*(2), e255. https://doi.org/10.5001/omj.2021.56

Tegegne, B. A., & Kebede, B. (2022). Probiotics, their prophylactic and therapeutic applications in human health development: A review of the literature. *Heliyon*, *8*(6), e09725. https://doi.org/10.1016/j.heliyon.2022.e09725

Tesmer, L. A., Lundy, S. K., Sarkar, S., & Fox, D. A. (2008). Th17 cells in human disease. *Immunol Rev*, *223*, 87-113. https://doi.org/10.1111/j.1600-065X.2008.00628.x

Vargas-Mendoza, N., Madrigal-Santillan, E., Morales-Gonzalez, A., Esquivel-Soto, J., Esquivel-Chirino, C., Garcia-Luna, Y. G.-R. M., Gayosso-de-Lucio, J. A., & Morales-Gonzalez, J. A. (2014). Hepatoprotective effect of silymarin. *World J Hepatol*, *6*(3), 144-149. https://doi.org/10.4254/wjh.v6.i3.144

Verma, N., Usman, K., Patel, N., Jain, A., Dhakre, S., Swaroop, A., Bagchi, M., Kumar, P., Preuss, H. G., & Bagchi, D. (2016). A multicenter clinical study to determine the efficacy of a novel fenugreek seed (Trigonella foenum-graecum) extract (Fenfuro) in patients with type 2 diabetes. *Food Nutr Res*, *60*, 32382. https://doi.org/10.3402/fnr.v60.32382

Verstockt, B., Salas, A., Sands, B. E., Abraham, C., Leibovitzh, H., Neurath, M. F., Vande Casteele, N., & Alimentiv Translational Research, C. (2023). IL-12 and IL-23 pathway inhibition in inflammatory bowel disease. *Nat Rev Gastroenterol Hepatol*, *20*(7), 433-446. https://doi.org/10.1038/s41575-023-00768-1

Wadhwa, R., Gupta, R., & Maurya, P. K. (2018). Oxidative Stress and Accelerated Aging in Neurodegenerative and Neuropsychiatric Disorder. *Curr Pharm Des*, *24*(40), 4711-4725. https://doi.org/10.2174/1381612825666190115121018

Wang, M. N., Liu, L., Zhao, L. P., Yuan, F., Fu, Y. B., Xu, X. B., & Li, B. (2020). [Research of inflammatory factors and signaling pathways in knee osteoarthritis]. *Zhongguo*

Gu Shang, *33*(4), 388-392. https://doi.org/10.12200/j.issn.1003-0034.2020.04.020

Wang, X., Wong, K., Ouyang, W., & Rutz, S. (2019). Targeting IL-10 Family Cytokines for the Treatment of Human Diseases. *Cold Spring Harb Perspect Biol*, *11*(2). https://doi.org/10.1101/cshperspect.a028548

Weber, R., Groth, C., Lasser, S., Arkhypov, I., Petrova, V., Altevogt, P., Utikal, J., & Umansky, V. (2021). IL-6 as a major regulator of MDSC activity and possible target for cancer immunotherapy. *Cell Immunol*, *359*, 104254. https://doi.org/10.1016/j.cellimm.2020.104254

Williams, J. A., Burgess, S., Suckling, J., Lalousis, P. A., Batool, F., Griffiths, S. L., Palmer, E., Karwath, A., Barsky, A., Gkoutos, G. V., Wood, S., Barnes, N. M., David, A. S., Donohoe, G., Neill, J. C., Deakin, B., Khandaker, G. M., Upthegrove, R., & Collaboration, P. (2022). Inflammation and Brain Structure in Schizophrenia and Other Neuropsychiatric Disorders: A Mendelian Randomization Study. *JAMA Psychiatry*, *79*(5), 498-507. https://doi.org/10.1001/jamapsychiatry.2022.0407

Wozniak, T. M., Ryan, A. A., & Britton, W. J. (2006). Interleukin-23 restores immunity to Mycobacterium tuberculosis infection in IL-12p40-deficient mice and is not required for the development of IL-17-secreting T cell responses. *J Immunol*, *177*(12), 8684-8692. https://doi.org/10.4049/jimmunol.177.12.8684

Xu, T., Guo, Y., & Qi, X. (2019). Ubiquitination-Mediated Inflammasome Activation during Bacterial Infection. *Int J Mol Sci*, *20*(9). https://doi.org/10.3390/ijms20092110

Yadav, M. K., Kumari, I., Singh, B., Sharma, K. K., & Tiwari, S. K. (2022). Probiotics, prebiotics and synbiotics: Safe options for next-generation therapeutics. *Appl Microbiol Biotechnol*, *106*(2), 505-521. https://doi.org/10.1007/s00253-021-11646-8

Yang, X., Zeng, J., Yu, X., Wang, Z., Wang, D., Zhou, Q., Bai, T., & Xu, Y. (2023). PCT, IL-6, and IL-10 facilitate early diagnosis and pathogen classifications in bloodstream infection. *Ann Clin Microbiol Antimicrob*, *22*(1), 103. https://doi.org/10.1186/s12941-023-00653-4

Yeung, Y. T., Aziz, F., Guerrero-Castilla, A., & Arguelles, S. (2018). Signaling Pathways in Inflammation and Anti-inflammatory Therapies. *Curr Pharm Des*, *24*(14), 1449-1484. https://doi.org/10.2174/1381612824666180327165604

Yshii, L., Pasciuto, E., Bielefeld, P., Mascali, L., Lemaitre, P., Marino, M., Dooley, J., Kouser, L., Verschoren, S., Lagou, V., Kemps, H., Gervois, P., de Boer, A., Burton, O. T., Wahis, J., Verhaert, J., Tareen, S. H. K., Roca, C. P., Singh, K., . . . Liston, A. (2022). Astrocyte-targeted gene delivery of interleukin 2 specifically increases brain-resident regulatory T cell numbers and protects against pathological neuroinflammation. *Nat Immunol*, *23*(6), 878-891. https://doi.org/10.1038/s41590-022-01208-z

Zarkovic, N. (2020). Roles and Functions of ROS and RNS in Cellular Physiology and Pathology. *Cells*, *9*(3). https://doi.org/10.3390/cells9030767

Zhao, Q., Liu, H., Tang, L., Wang, F., Tolufashe, G., Chang, J., & Guo, J. T. (2024). Mechanism of interferon alpha therapy for chronic hepatitis B and potential approaches to improve its therapeutic efficacy. *Antiviral Res*, *221*, 105782. https://doi.org/10.1016/j.antiviral.2023.105782

Zhao, X. L., Liu, Y. L., Long, Q., Zhang, Y. Q., You, X., Guo, Z. Y., Cao, X., Yu, L., Qin, F. Y., Teng, Z. W., & Zeng, Y. (2023). Abnormal expression of miR-3653-3p, caspase 1, IL-1beta in peripheral blood of schizophrenia. *BMC Psychiatry*, *23*(1), 822. https://doi.org/10.1186/s12888-023-05182-0

Zhao, Z., Ning, J., Bao, X. Q., Shang, M., Ma, J., Li, G., & Zhang, D. (2021). Fecal microbiota transplantation protects rotenone-induced Parkinson's disease mice via suppressing inflammation mediated by the lipopolysaccharide-TLR4 signaling pathway through the microbiota-gut-brain axis. *Microbiome*, *9*(1), 226. https://doi.org/10.1186/s40168-021-01107-9

Zheng, J., Zheng, S., Feng, Q., Zhang, Q., & Xiao, X. (2017). Dietary capsaicin and its anti-obesity potency: from mechanism to clinical implications. *Biosci Rep*, *37*(3). https://doi.org/10.1042/BSR20170286

Zhu, H., Cao, C., Wu, Z., Zhang, H., Sun, Z., Wang, M., Xu, H., Zhao, Z., Wang, Y., Pei,

G., Yang, Q., Zhu, F., Yang, J., Deng, X., Hong, Y., Li, Y., Sun, J., Zhu, F., Shi, M., . . . Zeng, R. (2021). The probiotic L. casei Zhang slows the progression of acute and chronic kidney disease. *Cell Metab*, *33*(10), 1926-1942 e1928. https://doi.org/10.1016/j.cmet.2021.06.014

Zhu, Q., Li, H., Zheng, S., Wang, B., Li, M., Zeng, W., Zhou, L., Guan, Z., Wang, H., Liu, Y., Gao, Y., Qiu, S., Chen, C., Yang, S., Yuan, Y., Zhang, H., Ruan, G., & Pan, X. (2022). IL-6 and IL-10 Are Associated With Gram-Negative and Gram-Positive Bacteria Infection in Lymphoma. *Front Immunol*, *13*, 856039. https://doi.org/10.3389/fimmu.2022.856039

Zhu, X., Sang, L., Wu, D., Rong, J., & Jiang, L. (2018). Effectiveness and safety of glucosamine and chondroitin for the treatment of osteoarthritis: a meta-analysis of randomized controlled trials. *J Orthop Surg Res*, *13*(1), 170. https://doi.org/10.1186/s13018-018-0871-5

Zivkovic, A. M., Telis, N., German, J. B., & Hammock, B. D. (2011). Dietary omega-3 fatty acids aid in the modulation of inflammation and metabolic health. *Calif Agric (Berkeley)*, *65*(3), 106-111. https://doi.org/10.3733/ca.v065n03p106

Zoi, V., Galani, V., Lianos, G. D., Voulgaris, S., Kyritsis, A. P., & Alexiou, G. A. (2021). The Role of Curcumin in Cancer Treatment. *Biomedicines*, *9*(9). https://doi.org/10.3390/biomedicines9091086

Zwicky, P., Ingelfinger, F., Silva de Melo, B. M., Ruchti, F., Scharli, S., Puertas, N., Lutz, M., Phan, T. S., Kundig, T. M., Levesque, M. P., Maul, J. T., Schlapbach, C., LeibundGut-Landmann, S., Mundt, S., & Becher, B. (2021). IL-12 regulates type 3 immunity through interfollicular keratinocytes in psoriasiform inflammation. *Sci Immunol*, *6*(64), eabg9012. https://doi.org/10.1126/sciimmunol.abg9012

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