

Review

Spirulina ingestion can potentially trigger Dermatomyositis: A call for research on an uncharted phenomenon

Running title: Spirulina and dermatomyositis

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Abstract

Dermatomyositis (DM) is an immune-mediated dermatological condition characterized by unclear pathogenesis. Several environmental factors have been implicated in its aetiology, including the microalga Spirulina. This dietary supplement has been proposed as a potential trigger for disease exacerbation or as an agent capable of initiating de novo DM. This review examines the current literature on the potential association between spirulina ingestion and the onset or exacerbation of DM and proposes directions for future clinical research.

Keywords- Diet, Supplements; Myositis, Nutrition

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I. INTRODUCTION

Dermatomyositis (DM) is an autoimmune disease affecting the skin and muscles, with distinctive rash formations and necrosis [1]. Shaped by different environmental, genetic, and immunological factors, studies investigating the cyanobacterium spirulina as a possible factor in DM reveal key aspects of its likely contribution to the disease's development. Ongoing research emphasizes spirulina's intricate interactions

with the immune system, especially its ability to influence immune-mediated inflammation, suggesting that spirulina ingestion may lead to an autoreactive immune response that worsens or triggers DM symptoms in some individuals

II. SPIRULINA INTAKE AS AN IMMUNOSTIMULATING FACTOR

The microalgae spirulina has been studied and often consumed by patients as an immune boosting dietary supplement. It has been proven to enhance both innate and specific immunity by promoting white cell production, mobilization and antibody production in animal studies [2]. Some propose that it is a generally safe immunomodulator and nutritious agent, with promising benefits against infectious and systematic diseases [3,4,5]. Others point out its potential immunostimulating and autoimmune-inducing properties, especially in autoimmune skin disorders such as DM. The contradiction in current literature is evident.

Several publications report activation of molecular mechanisms such as increased levels of specific cytokines linked to inflammation and oxidative stress

after spirulina intake, potentially triggering an autoimmune response in susceptible individuals. Identified mechanisms include the activation of pro-inflammatory cytokines and alterations in pro-inflammatory T cell, as well as a likely impairment of regulatory T cell responses. For example, Bax et al [6] report that spirulina stimulates production of Th1 cells cytokines, such as IL-2 and IFN- γ , along with other inflammatory cytokines such as IL-8, IL-12 and IL-18. Similar results were noted by Hirahashi et al [7]. This statement is also supported by a more recent publication [8] reporting an in vitro experiment demonstrating a clear connection between spirulina and DM stimulation. Their results included secretion of cytokines TNF- α , IFN- β and IFN- γ in DM peripheral blood mononuclear cells after spirulina exposure. Published data also point out that spirulina might cause oxidative stress, a known contributor to muscle inflammation and harm. The oxidative stress response is key in understanding how spirulina might affect DM. Increased levels of reactive oxygen species (ROS) were noted in participants taking high amounts of spirulina, indicating a disruption in their antioxidant balance and worsening symptoms related to the illness [9].

Genetic factors, existing health issues, and dietary choices may influence how spirulina interacts with the immune system and the likelihood of triggering DM. Concurrent medication may also alter the way spirulina accelerates DM. Bax et al [10], in another publication listing possible environmental factors triggering DM, specifically note several cases of patients suffering from DM flares or acute-onset disease after spirulina ingestion. Published data report the same phenomenon, which links spirulina ingestion not only with microscopical effects but also with clinical disease manifestations, thus increasing concern about the potential risk of spirulina exposure in patients susceptible or already diagnosed with DM. Other publications also stress the significance of individual differences in how people respond to spirulina. There was a reported case of DM stimulation by spirulina intake in an individual with confirmed TNF- α promoted polymorphism, which could be a predisposing factor for DM [11]. This suggests the urgent need for tailored dietary advice for those at risk of developing the disease.

This proposed aetiological link between spirulina intake and DM highlights the need for more research into how diet interacts with immune processes concerning DM. Moreover, little research data are provided on the amount of spirulina ingested by each

individual examined or on whether the DM triggering in each case was proportional to spirulina exposure, raising questions about minimal exposure and whether spirulina has a dose-dependent effect.

III. FUTURE RESEARCH AREAS OF IMMENSE INTEREST

Investigating spirulina as a potential trigger in DM highlights notable gaps in our understanding, especially concerning how spirulina might worsen or cause symptoms in affected individuals. More thorough research is needed to clarify how spirulina components interact with the immune system and trigger the inflammation linked to DM. The impact of genetic predisposition on individual responses to spirulina warrants additional examination, as there is currently insufficient research that considers both genetic and dietary factors. Clarifying the relationship between the two could be useful for developing more effective prevention and treatment strategies for those at risk of developing DM.

Besides genetics, there are also uncomprehended environmental factors related to spirulina. For example, the effects of lifestyle choices, other dietary habits and pollutants combined with spirulina intake has not been studied. Research that combines these environmental factors with spirulina consumption could provide crucial information regarding DM pathogenesis and how different elements contribute to its development.

Additionally, most current studies on spirulina and autoimmune diseases like DM often rely on translational and experimental studies or animal models. There are not many human clinical trials that look at the direct link between spirulina use and how often DM occurs or its severity. Long-term human studies with various groups of people, focusing in disease incidence and severity might provide an important understanding of spirulina's impact on DM over time, helping to clarify how exposure relates to when symptoms appear or get worse. Finally, there is an evident literature gap regarding the exact biological processes involved in how spirulina might cause DM symptoms. Both the specific components of spirulina that activate inflammation in DM, and the specific signaling pathways are still unknown. Identifying these pathways could not only improve our understanding of DM but could also help develop treatments to reduce the negative effects of spirulina on those at risk.

Answering these questions is important for improving our knowledge of spirulina's role in DM and creating effective management and prevention strategies.

IV. PROPOSED EXPERIMENTAL STUDIES

A combined approach of lab and animal studies could be used. Initial research will focus on how immune cells, especially T cells and macrophages, respond to spirulina extracts. This will involve examining changes in activation markers, cytokine levels, and immune signaling pathways that may be related to DM.

Researchers will conduct animal studies to assess the overall impacts of spirulina intake. They will use a known mouse model of DM to track symptom development after spirulina exposure. This will help clarify any connections between spirulina use and worsening symptoms of DM in a dose-dependent manner.

To initiate pathophysiological studies, molecular research will need to analyze the biochemical processes activated by spirulina. High-throughput sequencing and proteomic techniques will be used to find genes and proteins that change when spirulina is administered. These investigations will concentrate on pathways linked to autoimmune responses, such as those related to oxidative stress, cell death, and immune-mediated inflammation.

In addition, the proposed research will also include a clinical aspect, where samples from patients will be examined prospectively after exposure to spirulina. This part of the study will gather data on the dietary habits of individuals with DM and how it relates to their spirulina use. Researchers will evaluate markers of inflammation and immune activity alongside clinical symptoms to see if there is a connection between dose-dependent spirulina intake and worsening of DM in patients. This practical part of the research is crucial for confirming preclinical findings and aiding dietary guidance for those at risk of or diagnosed with dermatomyositis.

V. PRACTICAL APPLICATIONS

Examining spirulina as a potential trigger for DM has important consequences for clinical practice and

research. A collaborative approach involving immunologists, nutritionists, and rheumatologists can lead to a better understanding of how spirulina impacts DM pathways. Incorporating findings from recent studies that explain how spirulina influences immune system and potentially promotes inflammation could provide evidence-based guidelines for patients prone to autoimmune issues and improve both dietary and treatment plans. As knowledge grows, the aim should be to form a system that weaves dietary considerations into comprehensive treatment plans for dermatomyositis, ultimately improving patient care and management strategies.

Understanding the biological pathways by which spirulina may worsen or cause DM symptoms is vital for healthcare providers. As more people use natural products like spirulina, there is a strong need for ongoing training and education for healthcare workers on how dietary supplements relate to autoimmune diseases. Educational efforts evolving around both the beneficial aspects of spirulina and the possible adverse effects it could have on those at risk could include workshops, seminars, and updating medical education programs with recent research. Clinicians should be attentive to patients' dietary practices with DM, particularly regarding spirulina and similar supplements. This awareness can lead to more thorough patient assessment and information about the potential spirulina intake risks, and significant patient health and life quality improvement by preventing symptom onset related to this autoimmune disorder.

Researchers should aim at long-term studies that observe the effects of spirulina over time in people with dermatomyositis. Such studies would offer useful insights into spirulina's lasting effects and clarify cause-and-effect relationships. Building solid evidence will aid clinical practices and help patients make better dietary decisions.

VI. FINAL THOUGHTS

Spirulina, a nutrient-rich cyanobacterium, is noted for its potential health benefits, but its role as a possible trigger for DM symptoms should not be ignored. The connection between spirulina and DM reveals a complicated mix of biochemical processes and immune reactions that need more examination.

As researchers dive deeper into this connection, the biochemical attributes of spirulina, like its protein

makeup, antioxidant properties, and bioactive compounds that might affect immune function, should be considered. Oxidative stress caused by spirulina ingestion can potentially worsen autoimmune disorders. Specific peptides in spirulina could act like autoantigens, potentially leading to an unwarranted immune response in those genetically predisposed. This similarity at a molecular level could lead to the onset of DM by triggering autoantibody production and inflammation.

Another aspect to consider is the gut microbiome interactions with spirulina. New studies indicate that the gut microbiome might impact autoimmune disease severity, like DM. The effects of spirulina in gut health and microbial variety and function, which is often linked related to autoimmune responses should be further studied.

In summary, while spirulina has many health benefits, its possible role as a DM trigger calls for a careful diet for those already diagnosed with it or those prone to developing the disease. Future studies should aim to clarify how spirulina affects immune function and inflammation. Delineating these mechanisms at a molecular level is vital for identifying and treating groups of patients who might be more sensitive to spirulina, by providing better clinical practices and dietary recommendations.

AUTHOR CONTRIBUTIONS

All authors participated in manuscript preparation. All authors approved the final version of the manuscript.

CONFLICT OF INTEREST

All Authors declare no conflict of interest.

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