REVIEW ARTICLE

Comprehensive Review of the Safety and Efficacy of Thymosin Alpha 1 in Human Clinical Trials

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ABSTRACT

Objective • This study aims to assess the safety and efficacy of Thymosin Alpha 1 (Tα1) through a comprehensive narrative review of clinical studies involving over 11 000 human subjects in more than 30 trials. The focus was on Tα1's application in COVID-19, autoimmune conditions, and cancer treatment, with implications for future considerations.

Methods • We systematically searched articles relevant to critical studies on COVID-19, infectious diseases, cancer, and autoimmune diseases indexed on Pubmed, Google Scholar, and Cochrane Library. Our focus was on evaluating the safety and efficacy of Tα1 in human subjects. Clinical trials conducted worldwide involving diverse populations were analyzed to assess the safety and effectiveness of Tα1. The review examines explicit outcomes in over 11 000 human subjects, emphasizing its role in addressing COVID-19, autoimmune conditions, and cancer treatment.

Results • Contrary to the FDA's restriction on Tα1 and 21 additional peptides in 2023, our analysis reveals consistent evidence of Tα1's safety and efficacy. The peptide has demonstrated significant effectiveness in treating various conditions, including COVID-19, autoimmune disorders, and cancer. This review summarizes conclusions drawn from a comprehensive examination of clinical trials worldwide.

Conclusions • Based on substantial evidence from clinical trials, Tα1 emerges as a well-tolerated and effective immune modulator. The FDA›s restriction appears unfounded, as Tα1 has shown safety and efficacy beyond the initially specified conditions. Urgent attention and intervention are warranted to ensure the continued availability of this life-saving peptide through prescription. Therefore, it is recommended that the FDA permits 503A compounding pharmacies to compound Tα1, considering its potential to treat a variety of conditions effectively. (*Altern Ther Health Med.* 2024;30(1):6-12).

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INTRODUCTION

Thymosin Alpha 1 (Tα1) is a 28-amino acid peptide derived from calf thymus tissue by Dr. Allan L. Goldstein in the 1970s.[1] The synthetic form of this peptide, known as thymalfasin, has received approval in more than 35 countries for treating hepatitis B and C and as an immune enhancer in various diseases.[2] Despite being unapproved by the FDA in the USA, Tα1 gained FDA orphan drug approval from 1991 to 2006, allowing compassionate use in four clinical trials addressing conditions such as hepatitis B, thymus gland absence in children, DiGeorge Syndrome, hepatocellular carcinoma, and malignant melanoma.[3]

Tα1 plays a crucial role in immune system regulation, exerting influence over various immune cell subsets, including dendritic cells, T cells, and natural killer cells, integral to both innate and adaptive immunity.[4] Tα1 has been studied extensively for decades, showing its immunomodulatory effects, and is typically administered via subcutaneous injection, though intravenous administration is also possible. It has demonstrated a promising impact in enhancing T cell function and improving immune responses in both animal and human studies, and these findings hold significance for the treatment of diverse medical conditions, especially those associated with immune dysfunction. Human clinical trials have demonstrated that Tα1 possesses antiviral, autoimmune-mitigating, and anti-cancer properties, thereby suggesting its role in contributing to the treatment of widespread medical conditions.

This study specifically investigated the therapeutic domains of Tα1, examining its antiviral, autoimmune mitigating, and anti-cancer properties. The objective was to assess the contribution of Tα1 to the treatment of prevalent

Table 1. Safety Trials on Tα1 for Various Infectious Diseases (8075 Patients)

Author	Description	Sample Size	Adverse Effects
Shang et al. 2023[5]	Analysis of multiple studies on the effectiveness of Tα1 treatment for COVID-19.	5352	No allergic reactions or drug eruptions
Tuthill et al. 2023[8]	Application of Tα1 to patients on hemodialysis coinciding with COVID-19 infection.	194	No differences between the Tα1 group and placebo group with serious adverse effects
Wang et al. 2021[10]	Tα1 treatment in hospitalized patients with COVID-19.	275	No side effects were noted
Li et al. 2021[61]	Gender-specific markers in COVID-19 infected patients treated with Tα1.	127	No side effects were noted
Wu et al. 2013[11]	Tα1 for severe sepsis: a multicenter, single-blind, randomized and controlled trial	361	No Tα1 severe adverse event was reported
Liu et al. 2016[62]	Review of randomized controlled trials on Tα1 treatment in sepsis	530	No reported severe adverse event or treatment discontinuation with Tα1
Andreone et al. 1996[17]	Tα1 for the treatment of chronic hepatitis C	19	No side effects were noted
Rasi et al. 1996[18]	Tα1 and interferon for the treatment of chronic hepatitis C	15	No side effects were noted
Moscarella et al. 1998[19]	Tα1 and interferon for the treatment of chronic hepatitis C	17	No side effects were noted
Sherman et al. 1998[22]	Tα1 and interferon for the treatment of chronic hepatitis C	35	No side effects were noted
Ciancio et al, 2012[20]	Tα1 with peginterferon alfa-2a/ribavirin for chronic hepatitis C not responsive to IFN/ribavirin:	275	No side effects were noted
Poo et al. 2008[23]	Tα1 with peginterferon alfa-2a and ribavirin for chronic hepatitis C not responsive to IFN/ribavirin	40	No side effects were noted
You et al. 2006[13]	Tα1 and interferon-alpha in the treatment of chronic viral hepatitis B	62	3 patients had local site irritation. No other side effects were reported
Peng et al. 2020[14]	Meta-analysis on Tα1 plus Entecavir in Hepatitis B cirrhosis	572	Entecavir plus Tα1 led to a significant decrease in adverse events compared with monotherapy.
Lin et al. 2002[63]	Tα1 and famciclovir in chronic Hepatitis B	32	No side effects were noted
Zhang et al. 2009[16]	Meta-analysis on Tα1 plus Lamivudine in chronic Hepatitis B	295	No side effects were noted
Ramachandran et al. 1996[24]	Tα1, interleukin-2, and zidovudine in HIV	12	No side effects were noted
Garaci et al. 1998[25]	A randomized controlled study of zidovudine, thymosin-α1 and interferon-α in HIV	92	No side effects were noted
Chadwick et al. 2003[26]	Thymosin alpha 1 in augmenting immune reconstitution in HIV-infected patients with low CD4 counts taking highly active antiretroviral therapy	13	No side effects were noted
	Total Number of Patients: 8318		

Note: The table summarizes safety trials on Tα1 involving 8075 patients across various infectious diseases, including COVID-19, hepatitis, and HIV. The trials demonstrated a favorable safety profile with no significant adverse effects reported. The studies cover a range of conditions, indicating the potential of Tα1 in diverse therapeutic applications.

Table 2. Safety Trials on Tα1 for Cancer Treatment (2742 Patients)

Author	Description	Sample Size	Adverse Effects
Linye et al. 2021[64]	Tα1 therapy with Hepatitis B related hepatocellular carcinoma	468	No side effects were noted
Shuqun et al. 2004[45]	Combination transcatheter hepatic arterial chemoembolization with Tα1 on recurrence prevention of hepatocellular carcinoma	18	No adverse effects were reported.
Liang et al. 2016[44]	Tα1 therapy subsequent to radical hepatectomy in patients with hepatitis B virus-associated hepatocellular carcinoma	146	No adverse effects were reported
Stefanini et al. 1998[46]	Tα1 and Transcatheter arterial chemoembolization in hepatocellular carcinoma	12	No side effects were noted
Shuqun et al. 2006[65]	Tα1 and lamivudine for Hepatitis B associated hepatocellular carcinoma	16	No adverse effects were reported
Lopez et al. 1994[39]	Tα1, interleukin-2 and dacarbazine therapy in metastatic melanoma	46	No side effects were noted
Rasi et al. 2000[66]	Tα1, interleukin-2 and dacarbazine therapy in metastatic melanoma	20	No side effects were noted
Maio et al. 2010[41]	Phase 2 trial with Tα1 Dacarbazine with or without interferon-alpha for stage 4 melanoma	488	No adverse effects were reported.
Danielli et al. 2018[42]	Tα1 therapy with immune checkpoint Ab in metastatic melanoma	61	No adverse effects were reported. Follow up for more than 4 years
Schulof et al. 1985[29]	Randomized trial of Tα1 in non-small cell lung cancer	42	No adverse effects were reported.
Garaci et al. 1995[30]	Phase 2 trial with Tα1 and chemoimmunotherapy for advanced non-small cell lung cancer	56	Overall, treatment was well tolerated
Salvati et al. 1996[31]	Phase 2 trial with Tα1 and low dose interferon alpha after ifosfamide in non-small cell lung cancer	22	Hematologic toxicity was reduced with Tα1
Jiang et al. 2011[32]	Meta-analysis Tα1 plus cisplatin with vinorelbine or gemcitabine for non-small cell lung cancer	320	No drug-related serious adverse events
Guo et al. 2021[34]	Long-term survival with Tα1 therapy with non-small cell lung cancer after margin-free resected surgery	1027	No drug-related serious adverse events and no adverse events that led to Tα1 discontinuation
Dou et al. 2011[35]	Patients with invasive ductal carcinoma were evaluated in 2 groups, one receiving hormonal therapy and the other 4 cycles of chemotherapy, where all received Tα1	36	There are side effects from a depressed immune system, including less pain
Wenbo et al. 2023[67]	A prospective randomized controlled study of conventional and high dose Tα1 plus chemotherapy compared to chemotherapy alone	200	no discontinuation of treatment with reduced incidence of postoperative complications
An et al. 2004[36]	Clinical trial of Tα1 with chemotherapy for patients with colorectal cancer to reduce neurotoxicity	22	Tα1 reduced the neurotoxicity side effects with chemotherapy

Note: The table summarizes safety trials on Tα1 for cancer treatment, providing information on sample sizes, adverse effects, and references for each study. The total number of subjects across all studies is 3000.

medical conditions. Importantly, in its role in immune system regulation, peptide therapy, including Tα1, did not exhibit adverse severe reactions or known toxicity. The primary reported adverse event involved local injection site irritation, and most reported events were mild and transient and were also reviewed. Our results contribute to understanding the safety profile and potential benefits of Tα1 in clinical settings.

METHODS

This study employed a comprehensive search for articles relevant to critical studies on COVID-19 and other infectious diseases, including cancer and autoimmune diseases, indexed on Pubmed, Google Scholar, and Cochrane Library. The primary focus was to present an evaluation of the safety and efficacy of Tα1 in human subjects. Human trials utilizing Tα1 that could not be located or translated into English were excluded to maintain the study's integrity. Two tables were constructed to provide a detailed summary of reported side effects: Table 1 presented the side effects of Tα1 in Covid-19 and other infectious diseases, while Table 2 listed the peptide's side effects when used in the context of cancer.

DISCUSSION

Effectiveness of Tα1 Against COVID-19 and Infectious Disease

In the wake of the recent COVID-19 pandemic, which exposed the susceptibility of immune dysfunction, it becomes imperative to explore innovative approaches to enhance immune function. In January 2023, a meta-analysis encompassing over 5000 patient outcomes across nine studies investigated the effects of treatment with Tα1

compared to control or standard care. Notably, no serious adverse events related to Tα1 were reported. Subanalysis further revealed a mortality benefit among individuals aged 60 and above, those with critical COVID-19, and cases where Tα1 administration commenced early as opposed to late stages.[5]

One study[6] involved a pilot trial of Tα1 for the treatment of hypoxemic COVID-19 patients. Among the 23 patients receiving Tα1, any reported side effects were explicitly considered unrelated to Tα1. Additionally, a separate retrospective review[7] of 76 patients who received this peptide demonstrated a significant reduction in mortality and improved CD4+ T-cells, with no serious adverse events or discontinuation of therapy reported.

Furthermore, a randomized trial[8] involving 194 patients from 5 dialysis centers revealed that those who received Tα1 demonstrated efficacy in preventing the progression of COVID-19. The safety monitoring board reported no more serious adverse events than in the control group and observed fewer deaths. In late 2023, a systematic review[9] of 8 studies indicated that moderate to critical COVID-19 patients receiving Tα1 therapy experienced significantly lower mortality, with no mention of intolerance to this treatment. Notably, studies that did not find statistically significant benefits from using Tα1, such as the one conducted by Wang et al.[10], reported no serious adverse events or concerns leading to the discontinuation of therapy among the 149 participants in the Tα1 arm of the trial.

It is well-established that numerous infectious diseases lead to high mortality rates despite the current proven standard of care. Tα1 has been investigated in such contexts. In a multicenter randomized controlled trial[11] involving 361 patients with sepsis, no Tα1-related severe adverse events were reported, and therapy was not discontinued among the 181 treated, as reported by the university supervising the study. Subsequently, a meta-analysis[12] of 12 studies on septic patients found no Tα1-related adverse effects in two of the studies, with no mention of toxicity in the remaining trials, involving a total of 1480 participants. The conclusion of the meta-analysis highlighted lower mortality rates and recommended considering this peptide in future treatment strategies.

Concerning hepatitis B, numerous human trials employing Tα1 to treat hepatitis B have demonstrated significant benefits without serious side effects.[13,14] A study[15] investigating the combination of Tα1 and famciclovir revealed a greater reduction in HBV-DNA levels compared to famciclovir alone. Serological clearance of HBeAg was associated with the activation of HBV-specific Th1 cells, and no side effects were reported with Tα1.

Similarly, a meta-analysis[16] encompassing eight trials (583 patients in total, with 295 receiving Tα1 and lamivudine) indicated that the combination of lamivudine and Tα1 was significantly superior to lamivudine alone in terms of ALT normalization rate, virological response rate, and HBeAg seroconversion rate. No adverse side effects were reported with Tα1 in this meta-analysis. In another meta-analysis,[14] involving 310 patients (155 in the Entecavir plus Tα1 group and 155 in the Entecavir alone group) treated for 24 weeks, it was demonstrated that Entecavir plus Tα1 was significantly superior to Entecavir monotherapy in achieving undetectable HBV DNA levels. This meta-analysis also affirmed the safety of Tα1. Collectively, these studies consistently demonstrate positive outcomes and the safety of using Tα1 as a peptide treatment.

Earlier, when researchers initially explored the use of Tα1 to treat hepatitis C, a study[17] involving 19 patients found that Tα1 alone was not beneficial but was well-tolerated. However, the combination of Tα1 with Interferon in chronic hepatitis C demonstrated greater effectiveness than interferon alone. In an open-label trial,[18] 15 patients treated with a combination of Tα1 and Interferon for chronic Hepatitis C exhibited significant improvement. Six months after initiating treatment, seven patients (47%) tested negative for HCV RNA, and at the completion of the one-year trial, 11 patients (73%) had negative HCV RNA, including two individuals who had previously failed standard IFN treatment.

In another study,[19] 17 patients with chronic hepatitis C underwent treatment with a combination of Interferon and Tα1 (1 mg twice weekly), while another 17 patients received only Interferon. The treatment duration for all patients was 6 months, with a subsequent 12-month follow-up period. The results indicated that combination therapy demonstrated significantly higher efficacy than monotherapy in achieving biochemical and virologic end-of-treatment responses with no reported unwanted side effects.

In another study,[20] 552 patients with hepatitis C who had previously shown no response to interferon and ribavirin were randomly assigned to groups receiving either interferon, ribavirin, and Tα1 or interferon, ribavirin, and a placebo. Among them, 275 patients received Tα1 at a dose of 1.6 mg subcutaneously twice a week for 48 weeks. The inclusion of Tα1 in the standard care regimen did not lead to a reduction in HCV RNA levels, but it was well tolerated with no reported adverse reactions. Despite these less favorable outcomes, a separate case was documented involving two Koreans with hepatitis C, unresponsive to interferon and ribavirin, who exhibited a positive response to Tα1.[21]

Considering the earlier findings related to Tα1 and Interferon, three extensive studies were undertaken, including the United States Phase III trial, the Mexican pilot study, and the European Phase III trial. These studies aimed to assess the efficacy of Tα1 administered at a dose of 1.6 mg subcutaneously twice a week in challenging-to-treat patients with chronic hepatitis C who had not responded to previous antiviral therapy. The European Phase III study, comprising 275 patients, demonstrated that the addition of Tα1 to Interferon and ribavirin significantly reduced the relapse rate. Notably, Tα1 was found to be safe for use in the context of hepatitis C.[20-21]

The USA Phase III trial involved 109 patients, with 35 receiving Interferon and Tα1, 37 receiving Interferon, and 37 receiving a placebo. None of the groups received ribavirin. In

the Interferon and Tα1 group, 3 patients dropped out due to noncompliance with the protocol, a job change incompatible with the study regimen, and loss to follow-up. Tα1 was well-tolerated, and the combination of Tα1 and Interferon demonstrated lower HCV RNA, lower ALT, and improved histological activity index compared to Interferon alone.[22] A Mexican study by Poo et al.[23] evaluated triple therapy, including Tα1 with Interferon and ribavirin, in 40 Hispanic chronic hepatitis C patients who were non-responders. At the end of the 48-week study, nearly 50% had undetectable HCV RNA, and Tα1 was well-tolerated. Overall, Tα1 has been shown to be safe for use in hepatitis C.

In a clinical trial[24] involving patients with HIV, Tα1 demonstrated an increase in CD4 counts, specifically when administered in combination with zidovudine along with either interleukin-2 or interferon-α. A small study comprising 12 patients with HIV, given zidovudine, interleukin-2, and Tα1, exhibited no increase in HIV activation while showcasing an improvement in the CD4 count. Importantly, in this study, the peptide was well-tolerated. A multicenter Phase II randomized study[25] involving 92 patients with HIV revealed that the triple combination of zidovudine, Tα1, and alpha interferon resulted in a greater reduction in HIV RNA levels and an enhanced improvement in CD4 counts compared to other groups in the study.

In a randomized phase II clinical trial[26] conducted in 2003, highly active antiretroviral therapy (comprising multiple combinations of non-nucleoside reverse transcriptase inhibitors, nucleoside reverse transcriptase inhibitors, and protease inhibitors) was employed with Tα1 to assess its potential impact on improving CD4 counts. A total of 13 patients with HIV, already on highly active antiretroviral therapy, with viral loads below 400 copies/ml and CD4 counts below 200 cells/μ, received Tα1 for 12 weeks. Unfortunately, no improvement in their CD4 count was observed during this short 12-week study. It is important to note that the absence of enhanced CD4 counts could be attributed to the small sample size and the relatively brief duration of the study. However, Tα1 was well-tolerated in this trial.

Effectiveness of Tα1 Against Cancers

Early cancer investigations focused on Tα1 and its precursor, Thymosin fragment 5, conducted by the National Cancer Institute. These studies initially highlighted the favorable safety profile of thymic-based treatments, leading to the commencement of large-scale studies. Numerous clinical trials dating back to the 1980s have explored the use of Tα1 in combination with various chemotherapeutics compared to control groups. In a Cochrane review[27] from 2011 analyzing Tα1's use in randomized controlled trials of cancer treatment, three trials with specific safety monitoring included 56 patients. The reported adverse events, such as mild nausea, fatigue, and burning at the injection site, all resolved without sequelae.

Indeed, trends toward clinical benefits were observed in terms of reduced risk of mortality and higher disease-free survival. A 2019 review encompassing four clinical trials on non-small cell lung carcinoma (NSCLC) involving 320 patients treated with Tα1 revealed at least a trend toward treatment efficacy, and Tα1 was well-tolerated.[28-32] Subsequently, a more recent meta-analysis[33] of 27 studies reaffirmed the safety of Tα1 among NSCLC users. Out of these 27 studies, 20 utilized Tα1, while the remaining studies employed a different thymus peptide than Tα1. In 2021, a propensity score-matched analysis[34] involving 1027 patients found no new safety signals from Tα1 use, concluding it to be both safe and beneficial for patients.

Clinical trials have investigated the use of Tα1 in breast and colon cancer. In a study[35] involving 36 patients with invasive ductal breast cancer, those administered Tα1 alongside chemotherapy reported experiencing less pain and fewer side effects associated with a compromised immune system compared to those receiving chemotherapy alone. Another study,[36] focusing on 22 patients with advanced breast cancer, employed a dosage of 1.6 mg/day of Tα1 for 4 days before chemotherapy, followed by 1.6 mg twice weekly for 1-3 weeks afterward. Notably, this regimen demonstrated a reduction in neurotoxicity resulting from chemotherapy.

Regarding the mechanism of Tα1, a study[37] demonstrated that Tα1 induced apoptosis through the mitochondrial death cascade and inhibited the PI3K/Akt/mTOR signaling pathway in breast cancer cells. In the context of colorectal cancer, Tα1 was employed in a study involving 200 patients undergoing chemotherapy. The findings revealed that Tα1 improved the perioperative immune function of colorectal patients, reduced the incidence of postoperative complications, and increased the rate of disease-free survival, with no mention of discontinuing therapy.[38]

Melanoma is another cancer that has been extensively studied for the efficacy and safety of Tα1. Considering the rising concerns over side effects and diminishing efficacy of immunotherapy, this immune-modulatory approach is gaining attention. Earlier in the 1990s, Tα1 was investigated as a 'Biochemotherapeutic' to enhance the immune targeting of cancer. In one study[39] involving 46 patients with metastatic melanoma, there was no observed overlapping toxicity or interference between Tα1 and dacarbazine chemotherapy and no increased toxicity from the combination.

In a study[40] from 2015, Tα1 was highlighted as central and strongly recommended for cases related to melanoma. A larger study[41] utilizing Tα1 in melanoma, involving 488 patients treated with dacarbazine with or without interferon-alpha, demonstrated that Tα1 was safe, with no noted adverse effects. Another study[42] involving Tα1 in combination with an immune checkpoint blockade antibody, Ipilimumab, for metastatic melanoma followed patients for almost five years and revealed a longer survival rate with the combination of both medications, with no adverse effects noted for Tα1.

Hepatocellular carcinoma resulting from chronic hepatitis is another cancer investigated with Tα1 as a hopeful treatment option. Multiple clinical trials on hepatitis B and C, exploring the use and safety of this peptide, reveal a reduction in the hepatitis burden, thereby decreasing

progression to cancer.[43] Tα1 not only has the potential to contribute to cancer therapy directly but also to its prevention.

In a retrospective study,[44] 146 patients received Tα1 after hepatic surgery for hepatocellular cancer arising from hepatitis B. The results suggested that post-hepatectomy Tα1 therapy improves liver function and significantly prolongs recurrence-free and overall survival in patients with HBV-associated hepatocellular cancer. Several studies have explored the use of Tα1 for unresectable hepatocellular cancer in patients who are not candidates for surgery but have tumors small enough for ablative therapy or transarterial chemoembolization (TACE). TACE may prolong survival, and the addition of Tα1, along with an excellent safety profile, improved outcomes.[45-46] Additionally, incorporating Tα1 with lamivudine proves helpful in post-operative treatment to prevent recurrence.[47]

Tα1 Efficacy Against Autoimmune Diseases

Presently, there are over 100 autoimmune (AI) diseases, a significant increase compared to just a few decades ago.[48] Studies have illustrated that environmental toxins and the microbiome contribute to this rise. AI conditions are characterized by abnormal T-cell signaling, thus promoting systemic diseases. Furthermore, individuals with AI diseases have been noted to exhibit significantly lower circulating Tα1 levels than healthy subjects, highlighting immune dysregulation.[49] The growing trend of younger individuals developing AI conditions is alarming. The primary treatment approach involves immunosuppressives, which, unfortunately, do not effectively address the core of the disease and pose the risk of serious adverse events with prolonged use.[50]

Among AI diseases, Multiple Sclerosis (MS) affects more than 2.5 million people worldwide. In experimental animal models of MS, both Tα1 and Thymosin Beta 4 (a 43-amino acid peptide also derived from the thymus gland) have demonstrated efficacy in aiding myelin repair and providing neuronal protection. The authors suggest the necessity for human trials, considering this promising history.[51] Meanwhile, autoimmune disorders have already shown benefit from the effects of Tα1. For instance, a recent publication highlighted a pediatric patient with Crohn's disease who achieved complete clinical remission beyond one year after the introduction of Tα1, succeeding where other treatment options had failed.[52]

Apart from the recovery, no side effects were reported, demonstrating that Tα1 helped prevent unnecessary and harmful effects of long-standing immunosuppression. In another study[53] involving chronic idiopathic thrombocytopenic purpura, the combination of Tα1 with a high dose of dexamethasone proved more beneficial for 30 out of 39 (77%) patients compared to 12 out of 27 (44%) patients who received only a high dose of dexamethasone. Additionally, the Tα1 group exhibited a significantly lower relapse rate, with no documented cessation of therapy or harm noted.

The clinical applications for Tα1 are extensive, especially concerning the importance of recognizing the temporal association between autoimmune disease flares after COVID-19 vaccinations.[54] In line with its well-established safety profile, Tα1 not only proved to be safe but also showed some clinical benefits in most studies.

FUTURE IMPLICATIONS

Addressing Age-Related Decline and Enhancing Endogenous Function

Aging is associated with a decline in the immune system, leading to greater susceptibility to infectious diseases, a poorer response to vaccination, and an increased prevalence of cancer, autoimmune, and other chronic diseases. The state of the immune system can be assessed through a blood test measuring the CD4/CD8 ratio of T-helper cells to cytotoxic T-cells. A normal CD4/CD8 ratio ranges from 1 to 3, while a low CD4/CD8 ratio below 1 indicates an impaired immune system. The prevalence of an inverted CD4/CD8 ratio increases with age.[55] Tα1 has been demonstrated to improve the CD4/CD8 ratio, effectively enhancing endogenous immune function.[56]

Targeting Toll-Like Receptors and Enhancing Adaptive Immune Responses

Tα1 serves as a potent modulator of immunity and inflammation, operating as a toll-like receptor (TLR)-9 and TLR-2 agonist in both myeloid and dendritic cells.[57-58] By targeting TLRs, Tα1 can activate the adaptive immune response, which is crucial for combating viral, bacterial, and fungal infections, as well as cancers.[1] Furthermore, Tα1 has the capacity to elevate levels of IL-2, IL-10, IL-12, interferon (IFN)-α, and IFN-γ.[59] Its role in stimulating T-cell-dependent antibody production positions Tα1 as a potential vaccine adjuvant for enhancing responses to vaccines.

Activating T-Cells and Suppressing Inflammatory Responses

Tα1 plays an important role in activating T-cells into mature CD4 and CD8 cells with its immune-modulating properties. Tα1 directly stimulates natural killer cells and CD8 cells, enhancing their ability to eliminate virally infected cells. Moreover, its inhibitory impact on IL-1β and tumor necrosis factor-α contributes to a reduced inflammatory response.[60]

Harnessing Tα1 for a Paradigm Shift in Medicine

Aging contributes to immune dysfunction, marked by thymus gland atrophy and reduced Tα1 production. Research indicates lower Tα1 levels in individuals with autoimmune diseases compared to healthy controls. This finding prompts a paradigm shift in medical approaches. Rather than exclusively addressing infectious diseases, autoimmunity, or cancer, leveraging Tα1 emerges as a transformative strategy to maintain immune system health, ushering in a new era of medicine.

Tα1 Potential for Immune Dysfunction

Tα1 has proven beneficial for numerous patients struggling with compromised immune systems, spanning

infections, autoimmune diseases, and cancer. A survey of 503A compounded pharmacies, which dispense Tα1 prescriptions, revealed that over 500 000 Americans have embraced this treatment without encountering severe side effects. As systems biology medicine gains traction, there is a compelling case to research deeper into the potential of Tα1, advocating for its widespread utilization as a potent tool against immune dysfunction.

Safety and Future Promise of Tα1 in Addressing Immune Dysregulation

Tα1 emerges as a beacon of hope, highlighting its substantial benefits and flawless safety record. Notably, no documented concerns for harm or drug-drug interactions have been identified, positioning Tα1 as a promising solution for patients grappling with challenging medical conditions rooted in immune dysregulation. However, the disconcerting FDA scrutiny of Tα1, along with other proven peptides, raises significant apprehensions. Unlike many medications, Tα1 has navigated preclinical development, large phase 3 clinical studies, and current medical practice seamlessly, with no reported instances of misuse or harm in the extensive literature review.

The recent FDA ban on peptides, including Tα1, raises concerns about potential implications. If the ban persists, the public may turn to online sources that claim to provide peptides "for research purposes only," introducing uncertainty about their quality. This situation poses a significant risk to patient safety. Instead, ensuring a stable supply for healthcare providers by allowing regulated compounding pharmacies to continue their operations is a more prudent approach. These pharmacies adhere to rigorous quality control standards and accreditation requirements established by the FDA. Regular site visits, compliance with quality control measures, and specialty certifications are integral parts of their practice. Protecting the existence of 503A compounding pharmacies is crucial to ensure the continued production of safe and sterile Tα1 in accordance with the FDA's stringent standards.

CONCLUSION

In conclusion, Tα1 has demonstrated its safety with over 11 000 subjects enrolled and clinically evaluated in high-quality studies, with no significant harm ever reported. Tα1 has proven lifesaving when used to treat various conditions without resulting in long-term complications or interactions seen with other medications. Studies of Tα1 have increased exponentially, as reflected in the literature, supporting its continued use and exploration for additional treatment options. Post-marketing surveillance, based on the experience of more than 600 000 treated patients with this peptide, affirms Tα1's excellent tolerability. Discontinuing its compounding would likely cause more harm than good.

Therefore, clinicians should retain access to such treatment options and have the authority to prescribe them based on evidence-based medicine, free from undue influence. Unless there is a substantiated case against a therapy, the removal of the ability to compound or produce a substance like Tα1 is unwarranted. Numerous pharmaceuticals have gained approval with far less safety data, only to be withdrawn from the market later due to harmful effects. Disallowing this drug would create a double standard and raise ethical concerns. Tα1 should be permitted for compounding by a 503A compounding pharmacy because it holds treatment implications across multiple medical specialties and has established a long-term safety profile to meet patient needs.

COMPETING INTERESTS

The authors report no conflict of interest.

AVAILABILITY OF DATA AND MATERIALS

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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