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Methods of Prevention and Mitigation of Autoimmune Diseases - A Review of The Literature

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ABSTRACT

Introduction and purpose: Autoimmune diseases are conditions where the body's immune system is unable to distinguish between auto- and foreign antigens and mistakenly attacks its cells, tissues, and organs. In recent years it became major public health concern because of the increasing diagnosis rate. Currently, about 5% of the population in Western countries is affected by such diseases, more often in women population.

The exact cause of autoimmune diseases is unknown, although most probably it results from a combination of genetic predisposition, environmental risk factors and immune dysregulation. Development of autoantigen-specific lymphocytes and autoantibodies might be decisive in starting the process of autoimmunity. Most common medication used in autoimmune diseases treatment are nonsteroidal anti-inflammatory drugs (NSADs), glucocorticoids, disease-modifying antirheumatic drugs (DMARDs). Additionally, there is biological medication available for many of them. It is known that non-pharmacological interventions, such as specific diets, supplementation or physical exercise is useful to mitigate the disease or even to prevent the body from its onset.

Materials and methods: The data for the article was found using the PubMed and Google Scholar websites. The key words used for the search included: 'diet and autoimmunity', 'autoimmunity and estrogens', 'microbiota and autoimmunity'. Articles not written in English, conference abstracts only and duplicated papers were excluded.

Conclusions: There is still no cure for autoimmune diseases, although various prevention and mitigation strategies can help manage these conditions and improve quality of life for affected individuals. However, for the use of some of them, evidence-based recommendations are not available. This review highlights current non-pharmacological therapeutic options.

Key words: inflammation; autoimmunity; rheumatoid arthritis; gut microbiota; diet; cannabinoids

INTRODUCTION

Autoimmune diseases are conditions where the body's immune system is unable to distinguish between auto- and foreign- antigens and mistakenly attacks its own cells, tissues,

and organs [1]. In recent years, there has been an increase in the incidence in autoimmune diseases and currently about 5% of the population in Western countries is affected by them, more often in woman and are considered as the fourth leading cause of disability and leading cause of mortality for female population and the third leading cause of morbidity in the industrialized world [1, 2, 3, 4]. They encompass a broad range of diseases, including rheumatoid arthritis, lupus, and type 1 diabetes (T1D), psoriasis, colitis ulcerosa, Leśniowski-Crohn disease, among others. While the exact cause of autoimmune diseases is unknown, they are believed to result from a combination of genetic predisposition, environmental risk factors (including infections, exposure to harmful chemicals, infections, stress, shift work and smoking), and immune dysregulation [1, 2].

Many researches indicate that development of autoantigen-specific lymphocytes and autoantibodies are decisive to start an autoimmune disease By providing the energy and substrates for B lymphocyte activation, differentiation, and function cellular metabolism is essential to control B lymphocyte's immune reactions [1, 2]. Some healthy individuals can develop specific autoantibodies, without manifesting symptoms of a disease. It is also important to remember that one autoimmune disease increases the risk of developing other diseases from this group. It is estimated that overlap syndromes account for about 25% of autoimmune diseases [5]. For example, in people with vitiligo, thyroid function should be monitored, especially with the appearance of new lesions that do not go away after the tan has disappeared. This is because there is an increased risk of Haschimoto's thyroiditis or Grave-Basedows' disease [6, 7]. Another example is the frequent co-occurrence of rheumatoid arthritis and Sjogren's syndrome [5].

Autoimmune diseases often have a chronic course, which strongly affects the mental state of patients. Stress and mental disorders can also aggravate their course as well as promote their onset in predisposed individuals [8].

There is many methods to prevent and mitigate the autoimmunological processes. The aim of this review is to summarize current data about pathophysiology and non-pharmacological therapeutic strategies which could be helpful in managing autoimmune disorders, also those which need further study. Although pharmacological interventions are also crucial in the management of autoimmune disorders, these strategies are outside of the scope of this review.

Etiopathogenesis of autoimmune disorders and mitigation strategies

Pathophysiology of many autoimmune diseases is still unknown. It is postulated that the most important in their development are autoreactive B cells, which present self-derived peptides to autoreactive T cells and activate them to promote the generation of pathogenic autoantibodies

from B cells. In the process of B cell functioning and immune responses, regulation and reprogramming of metabolic pathways are important as they provide the necessary metabolic support. Imbalances in immunometabolism may lead to inducing autoimmune diseases [1]. Below are described factors contributing to the development of autoimmune diseases and ways to alleviate or prevent.

Genetic predisposition: Genetic predisposition is necessary to start this process. Many autoimmune diseases are associated with alleles from the major histocompatibility complex (MHC). However, the penetrance of the MHC-associated alleles is never 100%, even for monozygotic twins, because development requires additional environmental and/or genetic modifiers or requires specific T-cell receptor arrangements. Also involved may be dysregulation of genes or pathways regulated by the RUNX family of transcription factors, which plays a role in hematopoietic cell development, development of T cells in the thymus, chromatin remodeling, and gene silencing [9]. In the thymus also takes place the process of maturation of T cells, which leads to the remove autoreactive T cells by deletion or fate-diversion into regulatory T cells. Disturbances of physiological age-related thymus involution should be considered as an possible cause of autoimmunity [10].

Another genes and molecules are the human leukocyte antigen (HLA) region, the cytotoxic T-lymphocyte-associated 4 molecule (CTLA-4), lymphoid-specific phosphatase (LYP) protein, cytotoxic T lymphocyte-associated 4 (CTLA-4) [11, 12].

Estrogens: Autoimmune diseases are more common in population of women than men. Furthermore disease onset is often observed during periods of peak estrogen levels [3, 13]. Estrogens, especially 17-β estradiol (E2) and prolactin, act as enhancers of humoral immunity, and testosterone and progesterone as natural immunosuppressants [13]. The exact molecular mechanisms of how female hormones regulate the immune system are not completely known yet, studies show that they control development, homeostasis, gene expression, and signaling processes in T and B [14]. Estrogens acts on two genomic pathways: classical and non-classical. The first one binds to its cognate intracellular steroid hormone receptor–estrogen receptor (ER), which has two types identified as ERα and ERβ encoded by the Esr1 and Esr2 genes respectively. In the second one, ER bound to DNA can interact with other transcription factors, or the ER may act as co-factor with transcription factors including Specificity protein 1 (Sp1), activating protein 1 (AP-1), NF-κB and p300 proteins and thereby activate a large number of genes and pathways and the ligand structure and specific ER-subtype dependent activation of either. ERs are widely expressed in most cells in the immune system [14]. The exact effect of estrogen on autoimmune diseases has yet to be thoroughly investigated.

Diet: T-cells are derived from hematopoetic stem cells (HSCs) and matures in thymus. The impact of diet and changes in gut microbiota on HSCs to reverse or postpone immunosenescence has recently received much attention. It is suggested that certain periodic dietary restrictions prevent and/or reverse age-dependent immune dysfunction by killing autoimmune cells and activating HSC-dependent regeneration while minimizing the burden of the intervention and the side effects [15]. Many studies indicate that dietary restriction (DR) is an effective intervention to increase healthy lifespan in various model organisms. These regimens include caloric restriction (CR), intermittent fasting (IF), time-restricted feeding (TRF), restriction of specific macronutrients, ketogenic diets (KD), and periodic fasting (PF) or fasting-mimicking diets (FMDs) [15]. CR prolongs the lifespan, increased insulin sensitivity, stress resistance, reduced morbidity, and prevents many age-associated diseases [16, 17, 19]. CR induces anti-inflammatory, antioxidant, and neuroprotective effects. Is also associated with increased plasma levels of corticosterone and adiponectin and reduced concentrations of IL-6 and leptin [16]. However, studies of the effects of many dietary interventions on the immune system have yielded different results, with chronic calorie restriction resulting in both positive and negative effects on the immune system and immune responses. Additionally, CR requires significant life-style changes, making them difficult to adhere to, especially for frail patients and older individuals. Furthermore, studies on mouse models suggest, that for example in Multiple Sclerosis, DR and KD may alter the course of experimental autoimmune encephalomyelitis (EAE), while IF was shown to help with disease severity [15, 16]. In addition, periodic 3-day cycles of a FMD can be effective in ameliorating demyelination and symptoms [17]. Randomized control trial, published by R. J. Davies et all, about the impact of CR on systemic lupus erythematosus (SLE) showed that DR significant reduce of Fatigue Severity Score (FSS) scores in patients with fatigue [19].

Moreover studies on streptozotocin (STZ)-induced type 1 diabetic (T1D) rats models indicate that CR improves glycemic homeostasis and reduces oxidative stress and lipid peroxidation. CR inhibits up-regulation of inflammatory cytokines (IL-1β, IL-4, and IL-6) and TNF-α, activates IL-10 and haptoglobin in the plasma of streptozotocin-induced diabetic rats. In pancreas of tested diabetic rats, IF improved glucose tolerance, insulin sensitivity and percentage of apoptotic B cells in the pancreas [15, 18, 20]. Furthermore, diabetes can be exacerbate by an alteration in the dietary protein content, whereas high-protein diet can accelerate the onset of disease in spontaneous autoimmune models of the non-obese diabetic (NOD) mice [15, 20]. Besides, high-protein diet showed significantly better glucose tolerance and mean insulin secretion [21].

Human epidemiological studies are suggesting that early exposure to intact dietary protein (e.g., most infant formulas) are environmental risk factor for the development of insulin dependent diabetes mellitus (IDDM) [22]. On the other hand, randomized controlled trial conducted by Mikael Knip et all (JAMA, 2014) do not support the thesis, that hydrolyzed formula is beneficial in reducing the incidence of diabetes-associated autoantibodies after 7 years [23].

Dietary interventions are also effective in rheumatoid arthritis. Studies showed that fasting followed by one year of lactovegetarian diet leads to significant improvement in number of tender joints, Ritchie's articular index, number of swollen joints, pain score, duration of morning stiffness, grip strength, erythrocyte sedimentation rate, C-reactive protein, white blood cell count, and a health assessment questionnaire score [24, 25]. However the systemic review from Cochrane Database conducted by Kåre Birger Hagen indicate, that the effects of dietary manipulation on rheumatoid arthritis are still uncertain due to the included studies being small, single trials with moderate to high risk of bias, furthermore the potential adverse effects, such as higher drop-out rates and weight loss in the groups with dietary manipulation, should not be ignored [26]. Nonetheless, eating a diet high in raw or mildly cooked vegetables, especially greens and legumes, as well as adding spices like ginger and turmeric, might be beneficial for treating rheumatoid arthritis (RA). Seasonal fruits and probiotic yogurt, which are high in natural antioxidants and anti-inflammatory qualities, nutritional supplements such as multivitamins, vitamin D, and cod liver oil, should be included in the diet. Products that should be avoided by patients with RA are: meals heavy in salt, oils, butter, sugar, and animal products, as well as processed foods [27].

Antioxidants, such as beta-carotene, vitamin C (ascorbate), and vitamin E (alpha-tocopherol or gamma-tocopherol metabolites), also can be effective ingredients to reduce inflammation by inhibiting lipid peroxidation and inactivation free radicals. There is an inverse association between vitamin C intake and risk of Latent Autoimmune Diabetes in Adults (LADA), as well as with lower risk of T1D related to higher vitamin C intakes and higher plasma ascorbic acid levels [28, 29]. Serum alpha-tocopherol concentration at the baseline examination is also inversely associated with IDDM [30, 31].

Selenium (Se) is known as a supplement prescribed by endocrinologists to the patients with autoimmune thyroid disease. It is an essential trace mineral for human health with many pleiotropic effects raging from antioxidant and anti-inflammatory capacity to thyroid hormone metabolism [32, 33]. Currently it is recommended, that in order to achieve the maximal activity of selenoproteine such as glutathione peroxidase (GPX), in plasma or in erythrocytes,

it is necessary to intake with food between 55 and 75 ug of Se per day. Foods rich in Se are brazil nuts, oysters, tuna, whole-wheat bread, sunflower seeds, chicken, turkey, pork, beef, lamb and mushrooms. Some studies suggests, that Se supplementation decreased thyroid peroxidase antibody (TPOAb) and thyroglobulin antibody (TGAb) titers, result in a decreased dosage of levothyroxine (LT4), improve glandular echogenicity and thyroid function in patients with Haschimoto Thyroiditis [33, 34, 35]. Although, the quality of the evidence about the Se impact on autoimmunity is low [35].

Omega acids: One of the most studies supplements in autoimmunological diseases with several clinical trials conducted among adults over the years are omega-3 polyunsaturated fatty acids (PUFAs). PUFAs include eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) which are mainly derived from oily fish and fish oil supplements and alpha-linoleic acid (ALA) derived from plant sources [36]. In a systemic systematic review concluded by Aristea Gioxari et all (Nutrition, 2018), has been confirmed, that supplementation with omega-3 PUFAs leads to substantial improvements in the duration of early morning stiffness (EMS), pain levels, erythrocyte sedimentation rate (ESR), physical function, grip strength, joint tenderness and levels of leukotriene B4 (LTB4) in patients with RA [36, 37]. Another clinical trial carried out by Jill Hahn et all (BMJ, 2022) investigated whether vitamin D and marine derived long chain omega 3 fatty acids reduce autoimmune disease risk. As a result it has been shown, that supplementation with vitamin D at a dose of 2000 IU/day for approximately five years, alone or in combination with 1 g/day of omega 3 fatty acids (460 mg eicosapentaenoic acid and 380 mg docosahexaenoic acid) led to a lower incidence of confirmed autoimmune disease than placebo, while supplementation with omega 3 fatty acids alone did not significantly lower incidence of autoimmune disease [4].

Vitamin D_3: Vitamin D and its effect on the immune system is another substance that has been intensively investigated in recent years. The mechanism of reducing autoimmune disease incidence is related to the fact, that vitamin D receptors are found at high density on dendritic cells, T and B lymphocytes and macrophages, whose functions are dramatically affected by activated by vitamin D metabolite - 1,25-dihydroxyvitamin (1,25(OH)2D). These substance inhibits expression of interleukin 2 (IL-2), an important growth factor for T lymphocytes, increase production of anti-inflammatory regulatory T cells, and suppresses T helper 1 cytokines IL-12, interferon γ, and tumor necrosis factor (TNF), while increasing IL-4, IL-5, and IL-10. Furthermore, can inhibits inflammatory IL-6, an important factor stimulating T helper 17 cells, which play a role in autoimmune disease development [4, 28].

Crohns disease (CD) is also associated with vitamin D deficiency. The gene encoding the pattern recognition receptor NOD2 (also known as IBD1), which mutations contribute strongly to CD development, is a direct target of 1,25(OH)2D signaling [38].

Gut microbiota: Recently, more and more papers are appearing on the connection between gut microbiota and autoimmune diseases. Gut-Associated Lymphoid Tissues (GALTs) is the frontline of gut mucosal defense [39]. Commensal bacteria are required for structural development of GALTs, as well as the formation of gut secondary lymphoid organs such as Peyer's patches, and priming various immune cells for proper immune function [39]. Intestinal dysbiosis is associated with increased prevalence of immune mediated diseases. For example, some studies indicates, that there is decrease of Firmicutes/Bacteroidetes ratio in SLE patients and T1D patients, increased abundance of Methanobrevibacter and Akkermansia and decreased abundance of Butyricimonas in patients with MS. RA patients may present a decrease in Faecalibacterium and expansion of Eggerthella and Collinsella [40, 41]. The dysbiosis of intestine microbiota seem cause the modification of the local innate immune system, such as the TLR pathway or inflammasome, which would lead the changes in systemic resistant framework and result in an autoreactive resistant reaction [39].

There is many ways to modulate the gut microbiota, such as the administration of antibiotics, probiotics, prebiotics, synbiotics or fecal microbiota transplantation (FMT) [42]. FMT since 1958 is used as a treatment for pseudomembranous colitis, additionally is has been widely used for Clostridioides difficile infections [42].

Case study conducted by Yvette H. van Beurden et al showed, that treatment of Clostridioides difficile with FMT in patients with refractory celiac disease type II can help to mitigate the disease. The authors are speculating, whether altering the composition of the microbiota could also help restore villous atrophy [43].

Jiaqi Zeng et al published case report, which showed promising results of FMT treatment in patients with RA. In this case, a 20-year-old woman with no underlying disease, but with RA, after several episodes of flares, has been treated with FMT, which has been administered to the patient's colon with 300ml of fecal suspension via colonoscopy under anesthesia. After the procedure has been observed a great decrease in Health assessment questionnaire disability Index (HAQ-DI) and Disease Activity Score 28 (DAS28), as well as the titer of rheumatoid factor (RF). Additionally, the dosage of medications has been reduced [44].

Studies suggest that it may be very important to modulate the gut microbiota at very early age to reduce the burden of autoimmune disease. For instance, breastfeeding, due to its ingredients, such as oligosaccharides that serve as natural prebiotics, as well as

microorganisms like lactobacilli and bifidobacteria, is associated by a reduction in numerous autoimmune disorders like celiac disease and multiple sclerosis [45]. Clinical trial, conducted by M Kalliomäki et al, which assessed the effect on atopic disease of Lactobacillus GG given prenatally to mothers who had at least one first-degree relative with atopic eczema, allergic rhinitis, or asthma, and postnatally for 6 months to their infants, indicate that it is effective in prevention of early atopic disease in children at high risk [46].

However it is still not clear, whether the dysbiosis is a result of systemic immune alteration or the primary changes in the pathogenesis of the disease. Also the treatment with FMT requires high-quality, prospective, randomized, controlled trials with large samples for this disease [39, 44].

Mental disorders and stress: Many epidemiological studies indicate, that stress precede autoimmunological diseases occurrence and to exacerbate symptoms [47, 48]. The stress response is conducted by hypothalamic–pituitary–adrenal (HPA) axis and sympathetic nervous system (SNS). Glucocorticoid play important role in stress response and immune regulation, by decreasing immune response. Thanks to that, they are used to treat many autoregressive processes. Nevertheless, they can also enhance inflammation and immunity [47].

In autoimmune diseases, common are psychological symptoms, such as fatigue, loss of interest in daily activities, and cognitive deficits, but sometimes it is difficult to differentiate, whether these are symptoms of systemic disease or depression [49]. Furthermore, idiopathic major depression is associated with increased circulating proinflammatory cytokines, interleukin (IL)-1, IL-6, tumor necrosis factor (TNF)-alpha level, as well as their soluble receptors, and the acute phase protein, C-reactive protein (CRP) [50].

The importance of mental health in fighting diseases is commonly known. Studie conducted by A. Nevriana et al. found increase in risk for both juvenile idiopathic arthritis (JIA) and psoriasis if a parent suffered from anxiety, depression or drug and alcohol use disorders; increase in risk for T1D if the mother were diagnosed with depression or eating disorders; risk for T1D in offspring was observed for mothers with an eating disorder [51].

Cohort study published in JAMA in 2018 conducted by Huan Song et al, which examined the cohort included 106 464 exposed patients with stress-related disorders, with 1 064 640 matched unexposed persons and 126 652 full siblings of these patients. As the results they came to a conclusions, that exposure to a stress-related disorder was significantly associated with increased risk of subsequent autoimmune disease, compared with matched unexposed individuals and with full siblings [48].

Additionally, Randomized Control Trial published in “Lupus” in 2020 conducted an updated review on the impact on SLE patients with exercise interventions, psychological interventions, such as group psychotherapy, cognitive behavioral therapies, psychoeducation, mindfulness-based cognitive therapy, electro-acupuncture, relaxation, attention placebo, symptom monitoring support, education, minimal needling, isotonic and resistance exercise. Compared with the control conditions, non-pharmacological interventions were associated with a significant improvement in fatigue, anxiety and depression and improved pain after interventions, as well as improvement in overall quality of life. It is important to note, that there have been no improvement in disease activity after 5–52 weeks of non-pharmacological therapies [52].

Further studies are needed to better understand the underlying mechanisms.

Other mitigating strategies

***Yoga, Tai Chi*:** Many publications indicate the role of sports in mitigating inflammation in the body. A lot of focus has been to yoga and Tai Chi. Regular, long-term yoga practice can prevent the body in stressful situations against increasing the level of cortisol and decreasing the level of INF- α, IL-6 and TNF- α, additionally helps the body to maintain blood pressure [53, 54, 55, 56, 57]. Additionally, while increased level of CRP, fibrinogen and decreased level of albumins are signs of inflammation, there is a small study, which may suggest that hatha yoga can decrease fibrinogen and hs-CRP level, as well as increase albumin level [58]. Furthermore, practicing yoga can mitigate the symptoms of RA, especially by reducing pain, improving function, creating a positive mental state, can decrease DAS28 scores, morning stiffness and affected joints, but the most significant benefits were observed when yoga was practiced in combination of physical postures, regulated breathing, meditation, and yoga philosophy [59, 60, 61].

Cochrane Database Systemic Review investigated whether Tai Chi had an impact on disease activity in patients with RA. Unfortunately, it is uncertain to have any effect on clinical outcomes (joint pain, activity limitation, function) in RA. Furthermore, since all outcomes had very low-quality evidence, important effects cannot be confirmed or excluded [62].

Mindfulness: Mindfulness comes from centuries-old Buddhist traditions and should lead to greater acceptance and an overall sense of well-being. It is defined as the nonjudgmental awareness of the present moment, acknowledge of distressing feelings and emotions with less reactivity and judgment, with attention focused on the body and breath, allowing the mind to rest from rumination and worry [63]. There is many studies about its impact on immunity and autoagressive disease. Mindfulness technics appear to be associated with reductions in the

activity of the cellular transcription factor NF-kB, reductions in circulating levels of CRP, increases in CD4+ T cell count (in HIV-diagnosed individuals), and increases in telomerase activity, which is associated with biological aging [64, 65]. In summary, there are many evidences on yoga effectiveness in mitigating symptoms of inflammation and should be considered an add-on therapy for many of them, for example rheumatoid arthritis. Nonetheless, further research is necessary.

***Cannabinoids (CNB)*:** Due to legalization in increasing number of countries, Cannabis sativa have gained prominence in recent decades, especially because of its therapeutic potential in treatment of inflammatory skin diseases, such as psoriasis or atopic dermatitis or allergic contact dermatitis. From the C. sativa can be derived many different metabolites, however best known are THC and CBD. Since THC has psychotropic effects, therefore its distribution strictly regulated, CBD does not have such effects and has greater application freedom in the market. CBD has a relatively low bioavailability, since it is a lipophilic compound with low absorption after oral administration, therefore is suggested to be administered a transdermal [66]. It is important to mention that humans have endocannabinoid system (ECS) and recently it is suggested, that it has its own ECS, which plays a critical role in the maintenance of skin homeostasis and barrier function. It is also involved in the regulation of neuro-immunoendocrine skin functions. Disruption of skin ECS may cause disorders such as dermatitis, acne, and pruritus. CNB receptors have been found in epidermal keratinocytes, melanocytes, dermal cells, mast cells, sweat glands, hair follicles and cutaneous nerve fibers [67]. Additionally, in vitro studies showed that CBD cumulates in the cytosol of keratinocytes to a larger degree than in cell membranes [68]. CNBs seem to be effective option for treatment of pruriutis. Furthermore, several clinical studies have also shown a reduction in pruritus caused by dermatologic (AD, psoriasis, asteatotic eczema, and ACD) and systemic (uremic pruritus and cholestatic pruritus) diseases. In other researches, CNBs have been found to decrease the number of Th1 and Th17 proinflammatory cells and the production of the proinflammatory cytokines, IL-1, IL-12, IL-17, IFN-γ, and TNF-α in mouse models [69]. Nonetheless, most of studies on the use of topical cannabis has been performed in vitro or in vivo using animal models [67, 70]. There are a few small studies on a human population, which give reason to believe that the topical administration of CBD ointment, is a safe and effective non-invasive alternative for improve the quality of life in patients with some skin disorders, especially on inflammatory background [71]. Further studies are needed to understand the underlying mechanisms as well as to find better strategies for autoimmune diseases treatment with CNB.

Skin condition	Possible mechanism of action	Additional properties
Pruritis	decreasing xerosis	Emollient cream containing PEA - reduced subjective severity of itch
Acne vulgaris	Modulating cytokine production, T-cell responses, cell proliferation; antimicrobial activity against C. acnes, anti-inflammatory, anti-lipogenic, and collagen-promoting properties.	A 40% reduction in acne lesions after 12 weeks of treatment.
Allergic contact dermatitis	THC may inhibit the IFN-γ-dependent production of chemokines. CBD increased AEA levels and inhibited the production of MCP-2, IL-6, IL-8 and TNF-α.	
Eczema	Increased skin hydration (measured by change in capacitance of the skin surface)	
Psoriasis	Effect on keratinocyte proliferation - inhibition of cell proliferation, concentration-dependent and independent of CB1R/CB2R. Downregulation of keratins expression in situ.	Treatment with cream, soap and oil improved psoriasis symptoms as early as 2 days after beginning.
Atopic dermatitis	Acceleration of the recovery of the epidermal barrier function and anti-inflammatory effects; CB1R agonists suppressed mast cell proliferation	Dietary hempseed oil - improvement of skin dryness and itchiness; decrease in dermal medication usage. Emollient cream containing PEA - decreased severity, flare-ups and use of topical steroids, improved symptoms, disease tolerance and sleep.

Table 1. Impact of topical skin products containing CBD on inflammatory skin diseases [67].

CONCLUSIONS

The range of medication and methods used in the treatment of autoimmune diseases has grown significantly in recent years. Once an autoimmune disease has developed, the focus

shifts to managing symptoms and slowing disease progression. Non-pharmacological methods are important to mitigate the symptoms. On the first line are lifestyle modification, containing diet, sports, such as yoga, tai chi as well as mindfulness. Regular exercise, a healthy diet, adequate sleep, and stress management can all contribute to symptom management and improved quality of life. Physical therapy can help manage symptoms of certain autoimmune diseases, such as rheumatoid arthritis, by improving mobility and strength.

In conclusion, while there is currently no cure for autoimmune diseases, various prevention and mitigation strategies can help manage these conditions and improve quality of life for affected individuals. As research advances, it is hoped that more effective strategies for the prevention and treatment of autoimmune diseases will be developed.

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The authors deny any conflict of interest

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