Prevention of Premature Ovarian Failure (POF) With Red Bean Supplementation: Case Study of Patients with Systemic Lupus Erythematosus

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KEYWORDS

kidney beans, Nuclear Factor Kappa B (NFkB), Atretic follicles, Estradiol (E2), premature ovarian failure (POF), Systemic Lupus Erythematosus (SLE)

ABSTRACT:

Introduction: Premature ovarian failure (POF) in women with SLE is a complex condition with serious health consequences, including psychological distress, infertility, osteoporosis, autoimmune disorders, and an increased risk of death.

Objectives: This study aims to prove that red bean extract causes a decrease in NFkB, the number of atretic follicles, and an increase in E2 levels affect POF indicators in SLE.

Methods: The research was conducted in a proper experimental laboratory with a post-test-only controlled group design. The subjects were female Balb/c mice given peroral red bean extract at 50, 75, and 100 mg/KgBB doses. The data was analyzed using SPSS 16 for Windows. A comparative test was performed through ANOVA, and a post-hoc Tukey test was performed.

Results: This study proved that red bean extract caused a decrease in NFkB, the number of atretic follicles, and an increase in E2 levels affected POF indicators in SLE.

Conclusions: For clinicians and the public, red beans can prevent POF in SLE patients. Red beans can be used as a preventive effort and early treatment of POF, reducing the incidence of POF in people with SLE.

1. Introduction

Systemic lupus erythematosus (SLE) is a complex autoimmune disease that has the characteristics of involvement of various organs and will have a significant impact when it attacks vital organs such as the kidneys, cardiovascular system, and central nervous system with varying clinical manifestations [1], [2], [3]. Lupus comes from the Latin word wolf; doctors have used this term since the thirteenth century. The word erythematosus (from the Greek word erythros, meaning red) refers to the circular reddish color of the face caused by SLE. Lupus describes an erosive facial SLE reminiscent of a wolf bite. Autoimmune means that the immune system cannot distinguish between foreign invaders and healthy tissues of the body ("automatic" means "autonomous") and creates automatic antibodies that attack and destroy healthy tissues [4].

SLE is a complex autoimmune disease with characteristic symptoms related to various organs that can endanger the patient's life. Symptoms can range from constitutional symptoms to manifestations in various organs such as mucocutaneous, musculoskeletal, hematological, and reticuloendothelial manifestations, effects on pregnancy with an increased risk of complications such as preeclampsia, premature birth, and low birth weight as well as other manifestations including serositis, nephritis, neurological disorders, and other organ involvement. [5], [6]. The emergence of SLE disease is influenced by many variables, including genetics,

environment, and changes in the immune system [7]. The genetic contribution has an essential influence on the development and pathogenesis of SLE, as seen from the heritability, risk locus, correlation with phenotype, and heterogeneity across populations. So, people of African descent dominate the highest prevalence of SLE, while Asians and Hispanics are included in the middle level, and the lowest are Caucasians [8].

Specifically, SLE incidence occurs primarily in countries such as the United Arab Emirates, Barbados, and Brazil with an estimated 43.7 per 100,000 people and around 3.41 million people and most of the sufferers are women with a rate of 78.73 (ranging from 28.61 to 196.33) per 100,000 people, and a total of around 3.04 million people, while in men it is only 9.26 (between 3.36 to 22.97) per 100,000 people with a total of 0.36 million people [9]. The data shows that SLE suffers more from women than men in the productive age, which is around 15-44 years and 45-64 years, with a ratio of 9:1 [10]. There are sex hormones as the main factor, one of which is estrogen produced by the female ovaries and plays a role in the innate and adaptive immune response and the dysregulation of this mechanism that causes autoimmune disorders [11], [12].

Vigorous estrogen receptor activity increases SLE activity in women [13]. Women's reproductive function decreases caused by chronic inflammatory mechanisms due to an increase in NFkB, an autoimmune response to oophoritis, hyperprolactinemia, abnormal uterine bleeding (AUB), and the use of chemotherapy agents [14], [15]. Multiorgan dysfunction in women with SLE causes menstrual irregularities, ovarian dysfunction, decreased ovarian follicle reserves, increased atretic follicles, and decreased production of estradiol hormone as an indicator of premature ovarian failure (POF), which leads to the cessation of menstruation before the age of 40 [16].

Premature ovarian failure (POF) in women with SLE is a complex condition with serious health consequences, including psychological distress, infertility, osteoporosis, autoimmune disorders, and an increased risk of death [17]. In addition, the prevalence of premature ovarian failure in SLE patients is also higher than in the general population, which is 17% due to the administration of drugs used for therapy with a cumulative dose of cyclophosphamide (CYC) of more than 10 grams, so this is the most important independent risk factor [18]. Therefore, the administration of the drug harms women with POF with SLE.

Treatment of patients with premature ovarian failure in SLE requires a thorough therapeutic approach. One of them is Hormonal Replacement Therapy (HRT), which is used to reduce menopausal symptoms, including heat and night sweats, by giving estrogen and progesterone hormone replacements that are reduced in the female body based on age [19]. HRT should be given at the time the woman is diagnosed with POF and continue until menopause, but HRT can be discontinued if there is an ongoing risk [20].

In addition to hormone replacement therapy, there are other ways to treat patients with POF with SLE, namely through natural treatments focused on overcoming autoimmune conditions and inflammation. One of the natural treatments that can be done is to use red bean extract or Phaseolus vulgaris L, which is a significant source of carbohydrates, proteins, and bioactive molecules with high and sustainable nutritional value [21]. Not only that, kidney beans contain rich phenolic components, including phenolic acids, flavonoids, and viscous tannins as antioxidants, anti-inflammatory, and immunomodulating as well as anticarcinogenic and cardioprotective [22].

2. Objectives

This study aims to prove the effect of red bean extract in preventing premature ovarian failure in mice model lupus erythematosus through a decrease in NFκB, atretic follicles, and an increase in atretic follicle levels on POF indicators in SLE. Analyzing the phenolic components of kidney beans can prevent the expression of pro-inflammatory genes such as TNF-α, IL-1β, IL-6, and COX-2, which NF-kB regulates. With the decrease in NF-kB, it can prevent premature ovarian failure. The importance of this study is to overcome premature ovarian failure in patients with Systemic Lupus Erythematosus.

3. Methods

This study is a purely experimental laboratory using a posttest-only controlled group design. The research subjects used female Balb/c mice divided into five groups. The first group, the negative control group (K-), is female mice not injected and not given kidney bean extract. The second group, the positive control group (K+), is female mice given intraperitoneal injections of pristane, busulfan, and cyclophosphamide. The third group, the treatment group (P1), is female mice given intraperitoneal injections of pristane, busulfan,

cyclophosphamide, and red bean extract at 50 mg/KgBB. The fourth group, the treatment group (P2), is female mice given intraperitoneal injections of pristane, busulfan, cyclophosphamide, and red bean extract at 75 mg/KgBB. The fifth treatment group (P3) is female mice given intraperitoneal injections of pristane, busulfan, cyclophosphamide, and red bean extract at 100 mg/KgBB.

The treatment was processed for 30 days, and then the mice were sacrificed and measured for the expression of NFκB, Atretic Follicles, and Estradiol (E2) levels against the POF indicator in SLE. The comparative test used ANOVA followed by a post hoc Tukey test on regular and homogeneous data. The Kruskal-Wallis test, followed by the Mann-Whitney test, assessed abnormal data. Then, the data was statistically analyzed using the SPSS 16 for Windows software program.

4. Results

Each variable shows different results. First, the results of the ANOVA one-way test and the Tukey test on NF-kB expression variables in five sample groups showed a significant difference (p-value<0.05) presented on the histogram as follows (Figure 1):

Figure 1 Histogram of mean ± standard-deviation of NF-KB expression

Figure 1 shows the average NF-B expressionκ in the five groups of consecutive observation samples from left to right, namely (1) the negative control group (K(-)) is normal female mice (no treatment); (2) the positive control group (K(+)) was female mice given intraperitoneal injections of pristane, busulfan, and cyclophosfamid (SLE model in isolation); (3) the treatment group (P1) was female mice of the SLE model and were given red bean extract at a dose of 50 mg/KgBB; (4) the treatment group (P2) was female mice of the SLE model and were given red bean extract at a dose of 75 mg/KgBB; (5) the treatment group (P3) was female mice of the SLE model and were given red bean extract at a dose of 100 mg/KgBB.

Visible average bar expression NF-κB was highest in the positive control group, meaning the intraperitoneal treatment of pristane, busulfan, and cyclophosphamide in female mice showed NF-(B is high). Meanwhile, the mean lowest bars in the control group were negative, which means that normal shrinkage will show low NF-B expressionκ. Meanwhile, the dose of red bean extract that is considered effective in reducing NF-κB expression in female mice of the SLE model is a dose of 100 mg/KgBB. Because the mean expression of NF-(B in the P3 treatment group (0.90±0.37d pg/mL) showed a value that was not much different from the negative control (0.18±0.08a pg/mL). In addition, the mean value of NF-(B expression in the P3 treatment group was very close to the mean expression of NF-(B in the negative control group compared to the other treatment group. Based on the above analysis, it can be concluded that red bean extract (Phaseolus vulgaris L) prevents premature ovarian failure in mice of the systemic lupus erythematosus model through decreased expression of NF-κB.

Second, the results of the ANOVA one-way test and the Tukey test on the atretic follicles in the observation sample group are shown on the histogram (Figure 2) as follows.

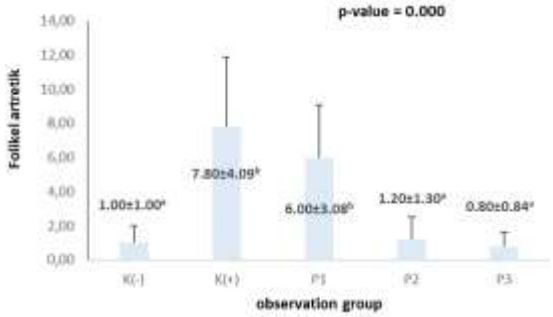

Figure 2 Histogram of mean ± standard-deviation of atretic follicles

Figure 2 shows that female mice had the highest average of atretic follicles in the positive control group given intraperitoneal injections of pristane, busulfan, and cyclophosphamide. The average stem was lowest in the P3 group, meaning that female mice of the SLE model who were given red bean extract at 100 mg/KgBB would show low atretic follicles. So, the dose of red bean extract that is considered effective in reducing atretic follicles in female mice of the SLE model is 100 mg/KgBB. This is because the average of the atretic follicles in the P3 treatment group (0.80±0.84a) showed no significant difference from the negative control (1.00±1.00a). In addition, the average value of the atretic follicles in the P3 treatment group was very close to the average in the negative control group compared to the other treatment groups. Based on this analysis, it can be concluded that red bean extract (Phaseolus vulgaris L) prevents Premature Ovarian Failure in mouse models of Systemic Lupus erythematosus through a decrease in atrial follicles.
Third, the ANOVA one-way test and the Tukey test on Estradiol (E2) levels in the observation sample group showed a significant difference in the average E2 level between the negative and positive control groups. Meanwhile, there was no significant difference between the positive control and P1 groups, but P2 and P3 had meaningful differences. The results are presented in the following histogram (Figure 3)

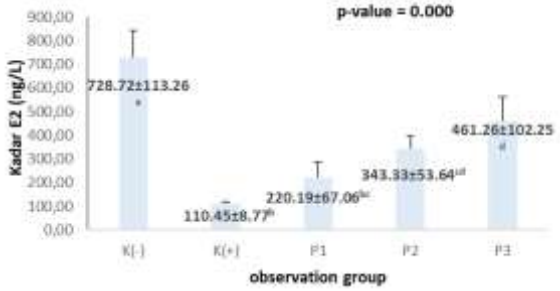

Figure 3 Histogram of mean ± standard-deviation of E2

Figure 3 shows that the highest average E2 levels occurred in the negative control group, which means that normal contraction shows high E2 levels. The low mean rods in the positive control group meant that the intraperitoneal pristane, busulfan, and cyclophosphamide treatment in female mice showed low E2 levels. Meanwhile, the dose of red bean extract that is considered effective in increasing E2 levels in female mice of the SLE model is a dose of 100 mg/KgBB. The average E2 level in the P3 treatment group (461.26±102.25d ng/L) showed a value not much different from the negative control (728.72±113.26a ng/L). In addition, the average value of E2 levels in the P3 treatment group was very close to the average E2 level in the negative control group compared to other treatment groups. Thus, from this analysis, it can be concluded that red bean extract (Phaseolus vulgaris L) prevents Premature Ovarian Failure in mouse models of Systemic Lupus erythematosus through increased E2 levels**.**

5. Discussion

SLE's cause is unknown, but it is suspected to be caused by many factors or multifactorial factors such as genetics, immunology, endocrine, and environmental factors. Over fifty genes or genomic loci have been linked to sickle cell disease (SLE), and the majority of these genes encode proteins essential for immune system operation. These genes are linked to the development of self-antigens, the activation of the innate and adaptive immune systems, and the immune system's reaction to external antigens. Rare conditions such as early complement component deficits of C1q, C1r, C1s (risk > 90%), C4 (50%), C2 (20%), and TREX1 are thought to carry a very high risk of developing SLE [23].

Women are 14 times more likely than men to acquire Klinefelter syndrome and 10 times more likely to develop SLE (47, XXY). indicates a possible link between X chromosome genes and SLE, while some research has not been able to conclusively determine the exact relationship. Hormonal factors are a major risk factor for SLE in women. [24]. Prolactin and oestrogen stimulate the generation of B-cell activation factors, alter lymphocyte and pDC activation, and enhance autoimmunity [25] [26]. It has been determined that certain environmental variables can result in aberrant immunological responses. One of the main causes of SLE is increased cell apoptosis, which is brought on by ultraviolet light and sun exposure [27]. Certain drugs can also result in self-antigen alterations and DNA demethylation, which can lead to lupus-like symptoms [28]. Procainamide and hydralazine have the highest prevalence of drug-induced lupus among the over 100 medications that have been related to it. Based on molecular mimicry, some viral infections have been linked to the SLE process. In

comparison to the general population, children and adults with SLE have higher rates of Epstein-Barr virus (EBV) antibodies [29]. The dose response deems smoking to be risky as well. Foods containing cannabis, insufficiency in vitamin D, exposure to silica, and various viral diseases are additional possible risk factors [30].

The pathogenesis of SLE is characterized by the formation of autoantibodies and disruption of the body's immune system that causes an unregulated inflammatory response. This results from genetic susceptibility, environmental factors, and hormonal influences [31]. Genes play a role in the immune autoregulation [32]. The autoantibodies and inflammatory conditions produced will initiate SLE disease and persist for a long time in the course of the disease [33].

The immune systems, both innate and adaptive, are involved in the pathophysiology of SLE. The Toll-like receptor (TLR) is necessary for the independent activation of the innate immune system. When exposed to extracellular DNA and RNA from damaged cells, cell membrane-bound TLR (TLR 2, 4, and 6) become activated. Pro-inflammatory mediators like IFN-b are produced by the transcription factors Interferon Regulatory Family (IRF-3), NF-κB, and MAP-kinase, which are activated by this. DNA demethylation of both foreign and self DNA/RNA (from viruses, for example) can result in the production of RNA-autoantibody interactions, such as antibodies to Ro, La, Sm, and RNP, and interferon-alpha. Meanwhile, single-stranded RNA activates endosomal TLR (TLR 7, 9) [30].

In the pathogenesis of SLE, NETosis is becoming increasingly identified. Several factors may activate neutrophils, such as cytokines, active platelets, and vascular endothelial cells, which discharge nucleate aggregates into the extracellular space on a regular basis. Thrombocysteine and vascular damage are facilitated by these nucleic aggregates, which also act as T-lymphocyte self-antigens and stimulate dendritic cells to create more interferon A [30]. B and T lymphocytes are crucial to the pathophysiology of sickle cell disease (SLE). The Antigen Presenting Cell (APC) on T-cells presents antigens produced from dying cells and injured cells. These T-cells in sickle cell disease (SLE) produce many cytokines as an expression of mutated genes. Less IL-2 and more modified regulatory T-cells are produced by T cells in SLE patients. The production of T cells is increased by an increase in IL-17 and IL-21, whereas the production of mononuclear cells is increased by an increase in IL-6, IL-10, IL-12, and IL-23 [34]. T-cells with defects are produced when Interfern-γ levels rise. T cells release CD40L and cytokines, which stimulate autoreactive B cells and result in the production of autoantibodies that are typical of SLE illness [35]. Furthermore, because there are no mechanisms for the functional neutralisation of autoreactive B cells, autoreactive B cells in SLE triggered by self-antigens cannot be eradicated. By exposing T-cells to lysically synthesised antigens, B-cells can also operate as APCs and trigger T-cell activation, so initiating a feedback loop in which B and T cells stimulate one another. Consequently, it increases autoimmunity [30].

Abnormalities in B-lymphocytes and T-lymphocytes are responsible for the immune system's lack or loss of self-tolerance, as self-reactive lymphocytes will function and survive [36]. Nuclear self-antigens stimulate these lymphocytes, and the antibodies produced fight the antigen [37]. When the antibody-antigen combination attaches to the B and dendritic cells' Fc receptor, it may be internalised. The nucleic acid component activates TLRs (Toll-like receptors) and increases autoantibody production in B cells (Figure 4). Additionally, this TLR signal will drive dendritic cells to release other cytokines, such as interferon, which may lead to an increase in the frequency of apoptosis. In essence, this repeated cycle of antigen release and immune activation will result in the production of autoantibodies of high affinity and end up in multi-organ damage [38]. External factors cause the antigen explosion. It produces antigen-antibody responses and strengthens nucleic acids in dendrite cells, B cells, and IFN-I production [39].

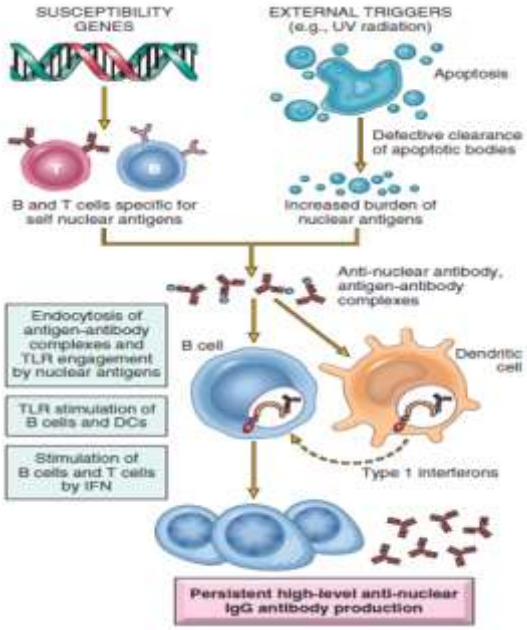

Figure 4 Pathogenesis Mechanism of SLE

The autoantibodies formed are pathogenic and cause organ damage due to the deposition of immune complexes, complements, and neutrophil activation, as well as altering the function of cells in apoptosis and cytokine production (Figure 4). Under normal conditions, the treated cells will be digested by macrophages in the early phase of cell death without causing inflammation. In addition, apoptosis will not activate dendritic cells that will present immunogens to T cells. In the case of SLE, the clitoris of the apoptosis cells will produce immunogens that will induce the autoreactivity of B cells and T cells so that they produce autoantibodies. Dendritic cells will also be active and produce pro-inflammatory cytokines such as TNF-α. In addition, Treg cells in SLE patients cannot efficiently suppress inflammation and proliferation of T cells. Dealing with immune complexes on the basal membranes of cells in different organs will cause local inflammation and tissue damage. Double-stranded (ds) DNA antibodies are an essential marker for SLE disease. Lupus nephritis begins with a complex immune storage containing anti-dsDNA in the renal parenchyma, activating the innate and adaptive immune system. The journey continues so that it causes the involvement of complement and toll-like receptors (TLRs), which can eventually cause the kidneys to become inflamed and develop fibrosis.

Anti-dsDNA can appear in about 80% of SLE patients and is one of the criteria for SLE by the American College of Rheumatology (ACR). Anti-dsDNA is related to the activity of SLE disease itself. As the disease progresses, there is a decrease in complement levels and an increase in anti-dsDNA levels. Anti-dsDNA itself can be measured using several methods such as Farr radioimmunoassay, Crithidia luciliae indirect immunofluorescence (CLIFT), enzyme-linked immunosorbent assays (ELISA), polyethylene glycol (PEG), fluorescence enzyme immunoassay (FEIA), and chemiluminescence assay (CLIA). Anti-dsDNA can be detected in a patient's serum as early as nine years before the diagnosis of SLE is established, but it can also be found in people who have not been affected by SLE. Anti-dsDNA levels are increased in cases of lupus nephritis.

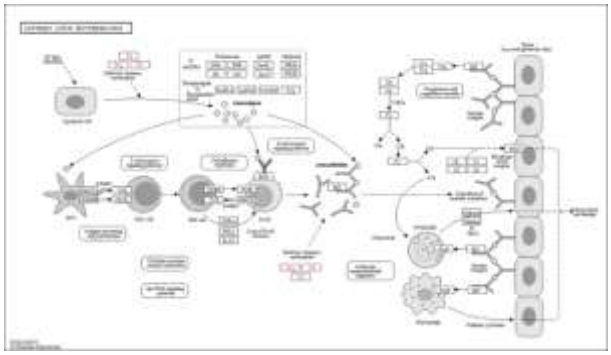

Figure 5 Immune system disorders in SLE

The production of IgG autoantibodies specific to antigens, such as DNA, cell nuclei proteins, and specific cytoplasmic components is increased in SLE. The main pathological findings in SLE patients are inflammation, vasculitis, deposition of immune complexes, and vasculopathy. Immune complexes consisting of autoantibodies and self-antigens are explicitly stored in the renal glomeruli and mediate systemic inflammatory responses by activating complements or through the R-mediated neutrophil and macrophage activation pathways by Fc. Activation of complement (C5) causes injury by forming membrane attack complexes (C5b-9) or by generating anaphylaxis and C5a cell activators. Neutrophils and macrophages cause tissue injury by releasing oxidants and proteases [40].

During the SLE disease, SLE activity alternates between the relapse (flare) and remission periods. However, the survival rate of patients has increased in recent decades due to early identification and treatment of the disease. Introduction of milder forms of the disease, advances in medical therapy, and better management of complications. The majority of SLE patients still experience repeated flares of the disease, which may adversely affect both short-term and long-term outcomes. The course of the disease is different for each individual, contributing to the variation in the patient's clinical manifestations.

The clinical picture of patients with SLE varies widely from very mild with only judicatory involvement to life-threatening with multiorgan involvement. In most cases, SLE manifests as a mild to moderate illness. The clinical manifestations of SLE are also. It is challenging to identify because they resemble many other diseases, so SLE is a great imitator involving all organ systems. The symptoms that appear in individuals with SLE range from constitutional symptoms to manifestations in various organs such as mucocutaneous, musculoskeletal, hematological and reticuloendothelial, neuropsychiatric, renal, pulmonary, cardiovascular, gastrointestinal, pregnancy, and other manifestations

Mukokutan manifestations are present in more than 80% of patients with SLE, so they are the easiest to identify. Photosensitive symptoms can occur, characterized by a new rash, recurrence of the previous rash, or an overreaction to sunlight, and may be accompanied by itching. The rash is often butterfly-shaped and occurs on the cheeks of the mammoth, and there is a joint in the nose. This rash is better known as a malar rash or butterfly rash. The incidence of this rash is quite common, namely in 25% of patients, and will disappear without any scar tissue remaining. Chronic skin SLEi is often found in skin areas exposed to the sun.

A frequent manifestation of female reproductive organs is menstrual disorders that range from amenorrhea to menorrhagia. First, amenorrhea can be caused by the direct impact of the disease itself, which can reduce ovarian reserve even in mild diseases. Second, in patients with severe manifestations and given treatment with alkylating agents such as cyclophosphamide (CYC), Where cyclophosphamide has a very high gonadotoxicity, amenorrhea can also occur. Cyclophosphamide users are at a higher risk of infertility and ovarian failure than patients who are not treated with it. Third, the function of the hypothalamic-pituitary axis is disrupted by chronic inflammatory states. This causes many pregnancies in SLE patients to have miscarriages, premature birth, intrauterine growth disorders, preeclampsia, and infant heart disorders [41].

An autoimmune systemic disease known as SLE is highly prevalent in women who are fertile. The impact of the hormone oestrogen on the immune system is one reason for the increased incidence of SLE in young women. In general, women's immunological responses to antigenic stimuli are stronger than men's. They may be more susceptible to autoimmune disorders than males because of this gender difference. An autoimmune systemic disease known as systemic lupus erythematosus (SLE) is more prevalent in women who are of reproductive age. The production of autoantibodies and the accumulation of antibody-antigen complexes in the organs' basal membranes, which trigger inflammatory and damage reactions, are important pathophysiological aspects of the illness. The high prevalence of SLE in young women is partly attributed to the effect of the hormone estrogen on the immune system.

The immune system is also affected by oestrogen, in addition to reproduction. There is a broad relationship between cellular immunity and oestrogen, according to recent research. During reproductive age, when the systemic effects of oestrogen prevail, women are more likely to suffer from SLE and other autoimmune illnesses. A few observational studies bolster the idea that oestrogen plays a part in the susceptibility to SLE. For instance, one study examined the impact of oestrogen on the immune system and compared the ratio of

males with SLE across various age groups. According to the findings, the ratio of male to female in children before puberty was 3:1; in adults, it rose to 15:1, but after menopause, it fell to 8:1.

In healthy individuals, T cells that control immunosuppressive regulation are crucial for preserving self-tolerance and averting autoimmune disease. Patients with SLE have less circulating T-reg cells (Mellor-Pita, Citores, et al. 2006), and treating them with 17-β estradiol further diminishes the quantity of these cells in vitro. During the disorder, there is an imbalance between T cells (Tregs) and T-helpers that produce IL-17 (Th17). Treg function is compromised, making it unable to oppose auto-reactive T cells. Th17 cells start to enter the target organ and, through controlling the production of IL-17 locally, destroy the organ. It seems that ER α and β play separate roles in the development of SLE. Erα antagonists can counteract the hyperresponsiveness of auto-antigen production in SLE patients to 17β-estradiol therapy. Animal research corroborated these results by demonstrating that, in mice undergoing ovariectomy, ERα agonist treatment was linked to a lower survival time and an earlier onset of lupus nephritis, while ER-β agonist treatment had virtually no influence on this parameter. Similar results were reported by Swenson and Gilkeson, who hypothesised that ER-β deficit had no effect on the disease, but that alpha ER deficiency in lupus women NZM, but not in men, had considerably longer survival, lowered proteinuria, and kidney pathology scores. These results imply that whereas ER-β activation appears to have minimal immunosuppressive influence on the illness, ERα activation plays a more dominating and immuno-stimulator function in estrogen-mediated lupus regulation.

Signs and symptoms of SLE, namely fever, fatigue, arthralgia, and weight loss. Fever in SLE should be distinguished from fever caused by infection, but both can coincide. Pain can affect small joints in the hands, wrists, and knees. Joint pain in SLE is asymmetrical, and the pain caused is not proportional to the degree of swelling. Weight loss can occur in active SLE, but weight gain can also occur in aspartic edema due to nephrotic syndrome as well as in people undergoing corticosteroid treatment. Symptoms on the skin can include malar rash, photosensitive, and discoid rash. Symptoms in the kidneys can include acute kidney failure or nephrotic syndrome. Symptoms of the nervous system and psychiatry include seizures and psychosis. Symptoms of the respiratory system include pleural effusion, pleuritis, pulmonary hypertension, and pneumonitis. Symptoms of the digestive system include nausea, vomiting, peptic ulcers, and peritonitis. Symptoms of the heart include pericarditis and myocarditis. Hematological signs include leukopenia, lymphopenia, anemia, and thrombocytopenia.

SLE is an autoimmune disorder whose cause is unknown. Experts estimate that the cause could be genetic processes and environmental factors impairing immune cells' ability to tolerate, producing several autoantibodies, activating complements, and depositing immune complexes [42]. This chronic inflammatory disease has a variety of clinical symptoms and is characterized by an autoantibody response to antigens in the nucleus and cytoplasm, which then attacks the cells of the skin, joints, kidneys, blood, lymph, lungs, and nerves.

Mayorga et al. [43] indicated that 71 SLE women, aged 17 to 45, had a 5.4% prevalence of POF in SLE. In the group not receiving cyclophosphamide therapy, the prevalence of POF was 0.6%, whereas in the group receiving cyclophosphamide therapy, it was 16.7%. There is no discernible difference in the prevalence of POF between female SLE patients and the general population. There is no statistically significant difference in the average menopausal age between women with SLE and those without SLE. AMH levels, however, were lower in SLE patients, which may be connected to how SLE affects ovarian reserve [44].

Based on the analysis of this study, the following conclusions can be drawn: First, red bean extract (Phaseolus vulgaris L) prevented Premature Ovarian Failure in mice of the Systemic Lupus Erythematosus model through decreased expression NF-κB. Second, red bean extract (Phaseolus vulgaris L) prevented Premature Ovarian Failure in mice of the Systemic Lupus Erythematosus model through increased E2 levels. Third, red bean extract (Phaseolus vulgaris L) prevented Premature Ovarian Failure in mice of the Systemic Lupus Erythematosus model through a decrease in atretic follicles. SLE researchers can develop this research that red beans (Phaseolus vulgaris L) can delay POF in people with SLE. For clinicians and the public, red beans can prevent POF in SLE patients. Red beans can be used as a preventive effort and early treatment of POF, reducing the incidence of POF in people with SLE.

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