Chapter 47

Use of Nigella Sativa (kalonji) against Arthritis

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ABSTRACT

Rheumatoid arthritis is a persistent inflammatory, gradually developing autoimmune disease with articular and systemic effects. It affects people of all races globally and has a prevalence of 0.5–1%. Numerous researches conducted in developing nations shows that disease prevalence is lower, between 0.1-0.5%. This illness has been observed to be more occurring in North America. However, black people in the Caribbean and rural sub-Saharan Africa have reported lower incidences. In the fourth century B.C., Hippocrates was the first to recognize rheumatic illnesses. The term "rheumatism" was first used in the first century A.D. by the Persian physician Guilliaume Baillou to describe a pain that was felt in all of the body's joints. It was described by him as musculoskeletal. It is a multifactorial disease characterized by pain and stiffness of joints. Its exact cause is not known but genetic and environmental factors are responsible for the ailment. Most RA patients have a homozygous form of the HLA-DRB1*04 epitope, which puts them at high risk of developing joint injury. PTPN22, STAT4 PADI4, , TNFAIP3, and TRAF1-C5 are additional loci linked to RA, while non-MHC risk alleles may account for just 3-5% of the genetic burden of RA. Activated T-cells with the MHC-shared epitope and HLA-DR4 alleles initiate the pathogenic process.

KEYWORDS
Arthritis, Rheumatoid, Kalonji, Nigella, Uses

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INTRODUCTION

Rheumatoid Arthritis is a persistent inflammatory, gradually developing autoimmune disease, damaging numerous joints with localized as well as generalized effects (González et al., 2009). Most patients with RA experience joint demolition, serious physical ailment and many co-occurring disorders. Its exact reason is not known, but environmental factors and genetic are responsible for ailment. Onset of the disease can be at any age, with incidence mostly in the age between 40-60 years (Choy, 2012).

Characteristics of Rheumatoid Arthritis

RA is characterized by pain and stiffness of joints with their gradual degradation resulting in disability. Its distinguishing features include synovial hyperplasia with migration of inflammatory cells, formation of new blood vessels, and destruction of bone and cartilage. RA is caused basically due to deregulation of immune system including its both compartments (Radu and Bungau, 2021).

Prevalence of Rheumatoid Arthritis

Rheumatoid Arthritis is discernible throughout affecting all races worldwide with prevalence of 0.5-1%. Its incidence in North America and Northern Europe lies between 0.5-1.1%. Southern Europe countries have incident rate of 0.3-0.7%. Various studies have been performed in developing countries that indicate a lower prevalence of disease i.e. 0.1-0.5% (Alamanos and Drosos 2005). A higher prevalence of this ailment has been seen in North America. Nevertheless, lesser incidence has been seen in rural sub-Saharan Africa and Caribbean blacks. In Middle East countries, the incidence of disease is 0.3-0.4%. In Asian countries, there is lower prevalence of disease. In Japan 0.3%, China and Indonesia 0.2-0.3%, Taiwan 0.3%, Philippines 0.2-0.3%, India 0.7 % and Pakistan has low incidence rate of 0.1% (Alamanos and Drosos 2005). RA is very prevalent inflammatory autoimmune disease in elderly people (Singh et al. 2016). Prevalence of Rheumatoid Arthritis increases significantly with age. Its incidence rate is only 0.3% in individuals below age of 35. However, rate is greater than 10% in senior individuals that are above 65 (Alamanos and Drosos 2005).

History

Hippocrates was the first who identified rheumatic ailments in fourth century B.C. The word rheuma was launched to specify feeling of pain throughout the joints of the body in first century A.D. Guilliaume Baillou who was a Persian physician first gave the concept of rheumatism. He defined it as a musculoskeletal (that affects muscles, tendons and ligaments of bone and joints) syndrome. Joseph L Hollander first launched the term rheumatology in 1949. Clinical illustration and definition of Rheumatoid Arthritis was first given by Augustin-Jacob in 1800. Definition of Rheumatoid Arthritis was further modified and was reported in 1988 (Alamanos and Drosos 2005).

Causes of Rheumatoid Arthritis

RA is a multifactorial disease influenced by both environmental and genetic factors, but its real cause is not known. Pathogenesis of RA involve role of B and T cells and organized interaction of cytokines. The vital cytokine (IL-17) that enhances synovitis, produced from reorganization of T cells into Th17. B cells perform a key function in pathogenesis by releasing cytokines, production of autoantibodies, and antigen presentation (Choy, 2012).

Genetic Factors

Majority of RA patients have antigenic determinant of the HLA-DRB1*04 in homozygous form, they are at high risk of having joint damage. Other RA-associated loci are PTPN22, TRAF1-C5PADI4, STAT4, and TNFAIP3, although non-MHC risk alleles may denote only 3–5% of the genetic load of RA. Commencement of the pathophysiological process is done by triggered T-cells, exhibiting HLA-DR4 alleles with the MHC-shared determinant. Responsible T-cell antigens are either single or numerous, including viral or bacterial products. Cross-reaction of T-cell antigen with self-antigen leads to production of cytokines either by the stimulation of cytokines or by direct cell-to cell contact (Choy, 2012).

Environmental Factors

Environmental factors impart a significant role in the onset, severity and the progression of rheumatoid arthritis (Edwards and Cooper, 2006). Although many infectious agents have been involved in the disease process, current data imply smoking as a significant environmental risk aspect for the progression of the RA in HLA-DR4-positive individuals. The relation between smoking and RA seems to be dose-dependent which is evident from hefty smokers (Alamanos and Drosos 2005). It has been suggested that smoking perhaps produce an ample source of neo-antigens to enhance further autoimmune reactivity (McInnes and Schett 2007). Rate of RA is two to three times more in women compared to men. Hormonal factors are responsible for high prevalence in women. Difference in development of arthritis in identical twins definitely indicate the significance of non-genetic factors in development of disease and for this, infectious agents are logical explanation (Oliver and Silman, 2006). Infectious agents such as bacteria may spread throughout the body including joints. Neutrophils, as a part of innate immune response, may move to the affected joints and deteriorate matrix components while attacking invading organisms (Burrage, Mix et al. 2006). Infectious agents like rubella virus, Epstein Barr virus have been found to be involved in disease process (Alamanos and Drosos 2005).

Dietary factors could remarkably increase risk of developing disease. Certain diets have been suggested that have potential to decrease risk of ailment such as Mediterranean diet. Other lifestyle factors that provide protective effects against Rheumatoid Arthritis include cooked vegetables, olive oil and fish. Their lifelong consumption could provide safety from disease (Alamanos and Drosos 2005). Many other elements such as socio-economic status, education and stress affect the incidence of disease (Tobón, Youinou et al. 2010).

Pathogenesis of Rheumatoid Arthritis

RA progression begins in synovial tissues neighbouring the joints and later, it moves towards cartilage. IL-1 and TNF-alpha play a role in arthritis. They lead to production of enzymes MMPs that have ability to destroy all parts of extracellular matrix (Luyten et al., 2006). MMP1 is mainly produced by synovial cells that cover the joints and MMP13 is produced by chondrocytes present in the cartilage. MMP13 plays a multiple role by degrading not only collagen but also aggrecan, a proteoglycan molecule. Other MMPs such as MMP2, MMP3 and MMP9 are also produced in increased amount in arthritis and they detoriate non- collagen parts present in joints (Burrage et al., 2006). NF-kappa B activation is required for expression of MMP1 and MMP13 as well as inflammatory stimuli such as Interleukin-6, Interleukin-1 and TNF-alpha. In response to high level of IL-1 and TNF-alpha, raised level of MMP1 and MMP13 collagenases has been observed in arthritic tissue (Vincenti and Brinckerhoff 2002). Disease begins with stimulation of innate immune comeback that mainly involves activation of antigen presenting cells (dendritic cells) by foreign agent such as bacteria or virus or in response to self-antigen. Antigen offering cells such as dendritic cells or macrophages present antigen to T cells. As a result, T cells produce IL-2 and IFN-gamma which permeate the synovial membrane (Choy, 2012). B cells contribute by production of autoantibodies which form large immune complexes that lead to release of pro-inflammatory cytokines such as TNF-alpha. T and B cell activation lead to increased production of cytokines and chemokines which in turn produce more T cells, macrophages, and B cells (Vita et al., 2002).

Role of Cytokines in Rheumatoid Arthritis

Cytokines are molecules of smaller size that bring about communication among different cells that ultimately leads to movement of the immune cells and inflammatory cells into the joints. As these cells move into the joints, they are activated

to generate products that results in tissue degradation (Arend, 2001). The actual job of these small molecules inside a complicated regulatory system are associated to particular immunological procedures that can enhance autoimmunity, chronic inflammation and tissue degradation (McInnes and Schett 2007). Hence the process of tissue degradation in rheumatoid arthritis requires the role of numerous cytokines which proceed in a complicated array as moderator of communication between different cells. Cytokines perform major part in the beginning of responsive synovitis, in the modification of this self-limited reaction into a hostile and tissue degradation procedure and further in the continuation of persistent synovitis. The same or dissimilar cytokines may play dynamic and complementary roles in these steps of the disease process (Arend, 2001).

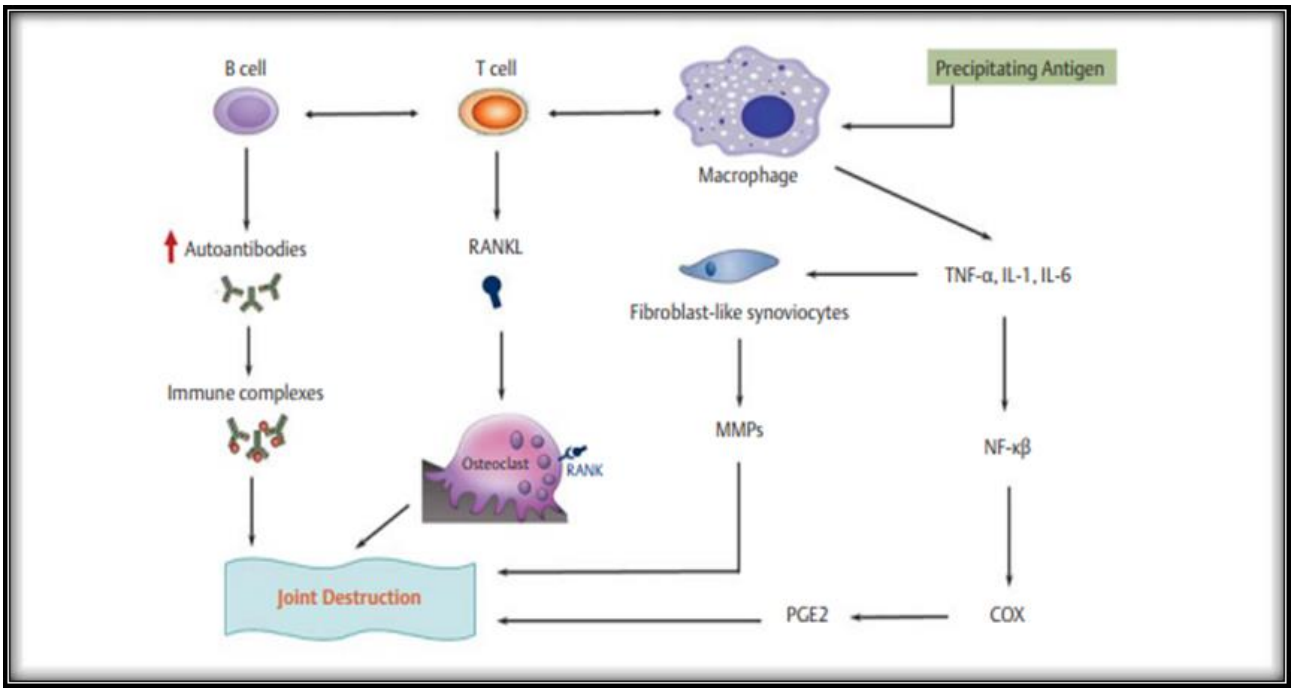

Fig. 1: Pathogenesis of Rheumatoid Arthritis

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Role of Pro-inflammatory cytokines- TNF- alpha and IL-1

These mediators perform a key function in the formation of the degenerative and inflammatory response. (Smolen, Redlich et al. 2005). Tumour necrosis factor-alpha, Interleukin-6 and Interleukin-1are the main moderators that are participating in migration of cells and inflammation (swelling) in rheumatoid arthritis (Choy, 2012). Tumour Necrosis Factor-alpha and Interleukin-1 perform major function in inflammation (swelling) and joint destruction that happens in rheumatoid arthritis. The pathological consequences of these mediators include migration of leukocytes into the synovium (leucocytes infiltration) which results in synovial hyperplasia, leading to activation of cells, destruction of cartilage and prevention of formation of cartilage matrix (Vervoordeldonk and Tak 2002).

IL-1

Interleukin-1α and Interleukin-1β are chiefly produced by macrophages; however, they can also be released by B and T lymphocytes and endothelial cells. Interleukin-1 can employ a range of generalized inflammatory responses such as inset of fever, wasting and also include formation of acute-phase proteins. Interleukin-1 also has ability to employ localized responses on cartilage as well as bone matrix synthesis. Furthermore, Interleukin-1 secondarily promotes joint damage by promoting fibroblasts to produce Interleukin-1, Interleukin-6 and Interleukin-8 (Dayer, 2003).

TNF-alpha

Tumour necrosis factor-alpha plays a more significant role than Interleukin-1 as it modulates discharge of pro-inflammatory cytokines in rheumatoid affected synovial tissue. It regulates release of other pro- inflammatory cytokines like Interleukin-6 as well as Interleukin-8. It promotes expression of prostaglandins (PGE2) and matrix metalloproteinase (MMPs) (Vervoordeldonk and Tak 2002).

IL-6

IL-6 specifically acts primarily on neutrophils with the aid of membrane IL-R which sequentially leads to swelling (inflammation) and joint damage by secreting proteolytic enzymes as well as reactive oxygen (RO) intermediates. (Choy,

2012). IL-6 promotes an acute phase reaction; however, in chronic(persistent) inflammation it has dual effects i.e. inflammatory and anti-inflammatory responses. Decrease amount of estrogen and androgen, that are also present in patients suffering from rheumatoid arthritis are related to raise levels of IL-6 (Hashizume and Mihara, 2011)

Role of Anti-inflammatory cytokines

These mediators are mostly considered as having immunoregulatory as well as inhibitory features. These cytokines are actually a chain of immunoregulatory molecules that have potential to regulate response of pro-inflammatory cytokines. In general, cytokines usually act in combination with particular cytokine inhibitors and receptors to control immune response in humans (Opal and Depalo 2000).

IL-4

IL-4 revert back cartilage degeneration generated by pro-inflammatory cytokines, impediment of angiogenesis (formation of new blood vessels); and bone resorption (Mobasheri, 2013). It performs a major role by deregulation of pro-inflammatory cytokines and aids to promote Th2 response (Dong et al., 2018).

IL-13

Interleukin-13 impedes secretion of various cytokines as well as chemokines. Interleukin-13 also has a pro-angiogenic response because it can trigger endothelial chemokines (Peluzzo and Autieri, 2022)). It performs a key role in deregulation of pro-inflammatory cytokines ((Hussein et al., 2021). It also has inhibitory characteristics similar to that of Interleukin-4. Its presence can be confirmed by immunostaining in synovial membrane of RA patients (Feldmann, Brennan et al. 1996).

Role of Regulatory Cytokine

IL-10

Interleukin-10 inhibits secretion of Interleukin-1 and Tumour Necrosis Factor-alpha with aid of Rheumatoid Arthritis mononuclear cells and impede cartilage damage. It can also inhibit release of Matrix Metalloproteinases. Interleukin-10 also prevents osteoclast growth and hence osteopenia (Szekanecz, Koch et al. 1998). It also perform a role in deregulation of pro-inflammatory cytokines and impediment of T-lymphocyte reaction (Isomäki and Punnonen 1997). Interleukin-10 is composed of two-fold features associated with development of inflammation (swelling) because it has both pro-inflammatory and anti-inflammatory features (Bevaart, Vervoordeldonk et al. 2010). Interleukin-10 also performs a regulatory function in progression of rheumatoid synovitis, based on the phase of disease (Arend 2001). It has significant anti-inflammatory as well as immunoregulatory features (Feldmann, Brennan et al. 1996).

Role of NF-kB in Rheumatoid Arthritis

Switching on of the NF-kB transcription family with aid of nuclear displacement of cytoplasmic network perform a key function in inflammation by its capability to enhance transcription of pro-inflammatory genes. It is thought to be a significant component giving rise to inflammation in chronic ailments such as Rheumatoid Arthritis (Tak and Firestein 2001). NF-kB is greatly switched on in synovial membrane of patients suffering from Rheumatoid Arthritis and may be a crucial element shielding cells from apoptosis, hence bringing about synovial hyperplasia (Tak, Gerlag et al. 2001).

Treatment Modalities for Rheumatoid Arthritis

Variety of drugs and anti-inflammatory agents account for the panacea of arthritis are accessible in the market. Some of them target cytokines, while others target related enzyme or proteins in inflammatory disease. Before discussing mode of action of non-steroidal drugs. It is important to first discuss the major targeted inflammatory protein and its function in the body.

Cyclooxygenase

Cyclooxygenase (COX) is the enzyme that assist in the catalysis of arachidonic acid in the biosynthesis of the prostaglandins (PGS) (Fitzpatrick, 2004). Metabolic products of arachidonic acid have significant role in various processes occurring in living organism including immunological and inflammatory functions, angiogenesis, ovulation and platelet accumulation in the body. There are two basic kinds of Cyclooxygenase-1 (COX-1), Cyclooxygenase, and Cyclooxygenase-2 (COX-2). COX-1 is present in almost every cell type including cells of duodenum, jejunum, ileum, renal cells, cells of large intestine and cells of stomach and lungs. The main role of COX-1 is to produce cytoprotective prostaglandins including PGE2 and prostacyclin, which play crucial role in maintaining probity and integrity of gastrointestinal mucosa (Fitzpatrick, 2004)**.** COX-2 is not produced continuedly in every cell type. It is produced because of some stimuli and expressed in specific cells only. COX-2 is used for signaling pain and inflammation. Some intracellular and extracellular stimuli are needed for its propagation. Following stimuli are responsible for the expression of COX-2 enzyme. LPS (lipopoly-saccharide) of bacteria, tumor necrosis factor (TNF), serum, converting growth factor alpha (TGFa), epidermal growth factor, interleukin like IL-1, retinoic acid, arachidonic acid, platelet activating factor (PAF) and endothelin. Following treatment, COX-2 level returns to normal within 24 ± 48 h. Its high level for longer duration causes serious complications in the body(Chen, 2010).

Nonsteroidal Anti-inflammatory Drugs (NSAIDS)

Studies have shown that Nonsteroidal anti-inflammatory drugs (NSAIDS) target the prostaglandin synthetase in the cyclooxygenase pathway. In Stomach, prostaglandins secrete bicarbonate and mucus, thus maintain mucosal cell turnover and mucosal blood flow. Inhibition of prostaglandin synthesis in stomach result into mucosal injury and gastric ulceration (Adinortey et al., 2013). Their way of targeting COX-1 is either by covalently modifying the enzyme or by competing for active site as a substrate. Prostaglandins are involved in physiological function of body; therefore, their blockage leads to chronic and undesirable side effects in the body. Gastrointestinal ulceration, bleeding and perforation are the life threating side effects of NSAIDS. It has been reported that frequent and daily users of NSAIDS have a greater chance of developing gastrointestinal and renal problems as compared to non-users. The rate of getting gastrointestinal complications is threefold high in daily users. PGI2 or PGE2 produced as a result of loss of COX-1 activity in stomach leads to chronic and severe gastric mucosal damage and ulceration in stomach (Wallace and Vong, 2008)

Nigella Sativa

Characteristics

Nigella sativa also known as kalonji, black cumin, charnushka, belongs to Ranunculaceae family is a flowering plant indigenous to Eastern Europe and western Asia, but can be easily full-grown in other areas like Europe, North Africa and Myanmar. It enhances the taste in different cuisines. The Nigella genus is miniature of the Latin word niger "black" which refers to the tint of the seed. The particular label sativa is translated as "cultivated "In English language, Nigella sativa is also known as by the variety of the names such as black caraway, black cumin, black seed and fennel flower.

Description

The average size of *Nigella sativa* plant reaches up to 20–30 cm (7.9–11.8 in) tall and they possess sharply divided and linear leaves but they are not threadlike. The delicate white and pale blue flower having five to ten petals can be seen on the tiny plant. The fruit of *Nigella sativa* is characterized as huge in size and pumped-up capsule comprised of three to seven integrated follicles (El-Morsy and Osman, 2021). Each fruit encompasses a massive number of seeds which put to use as spice for cuisines and sometimes in the substitute of *Bunium bulbocastanum* (black cumin).

Culinary Use

The dry-roasted seeds add taste to meal. The black seeds are also used as essence in bread products. In Bengali cuisine, the spice mixture (panch phoron) also contains these seeds. Nigella enhances flavour in tresse cheese, a braided string cheese called majdouleh in the Middle East. It is also marked safe for use as a spice, natural seasoning, or flavouring by The Food and Drug Administration of United States and it includes Nigella sativa in Generally Recognized as Safe (GRAS) list.

History

The medievalism evidence of *N. Sativa* cultivation traces back about three thousand years. These seeds were found in different sections of the world like ancient Egypt and the Tomb of Tutankhamun. *N. sativa* may have been used to flavour food in the condiment of the Old World. The Muslim physician Avicenna pronounced *N. Sativa* as a panacea for dyspnea in his The Canon of Medicine. In the Middle East, *N. Sativa* was used as local medicine.

Chemical Nature

Out of total conformation of *N. Sativa* seeds, 32% to 40% are oils, these comprise of Linoleic acid, Palmitic acid, Oleic acid, and Trans-anethole. In the minor ingredients, it includes Nigellidine, Nigellicine, and Nigellimine N-oxide. While from aromatics it possesses thymoquinone, p-cymene, Dihydrothymoquinone, Carvacrol, α-thujene, α-pinene, Thymol, β-pinene and Trans-anethole. Protein and various alkaloids are existing in the seeds. quinone, p-cymene (7%-15%), Carvacrol (6%-12%), 4-terpineol (2%-7%), t-anethol (1%-4%), Sesquiterpene longifolene (1%-8%) α-pinene and Thymol etc (Mukhtar et al., 2021). Furthermore, *N. Sativa* seeds tolerate potential to anticancer agent such as alpha-hederin, a water soluble pentacyclic triterpene and saponin. Additionally, some compounds e.g. Carvone, Limonene, Citronellol were also found in minor amounts. The pharmacological properties of *N. Sativa* are because of quinine constituents. On stowing, TQ yields Dithymoquinone and higher Oligocondensation products. The proximate composition of seeds of N. Sativa shows that protein is 26.7%, fat holds 28.5%, carbohydrates are 24.9%, and crude fibres maintain 8.4% and total ash accounts for 4.8 %. The seeds are also bearing good number of various vitamins and minerals like Cu, P, Zn and Fe etc (Albakry et al., 2022).

Traditional Use

N. sativa has marked for traditional use such as for the curing of a variety of diseases relating to digestive tract, respiratory system, liver and kidney function, cardio vascular system as well as for general well-being.Avicenna mentions in the "The Canon of Medicine" that black seeds integrate the body's energy and aid in recovery from fatigue. In Indian and Arabian civilization, Black seeds and their oil create a long history of folklore usage as food and medicine. The seeds have been traditionally used in Southeast Asian and the Middle East countries for the handling of several diseases and ailments counting asthma, rheumatism, bronchitis, and related inflammatory diseases. Its other uses earned Nigella the Arabic approbation 'Habbatul barakah', symbolizing the seed of blessing (Nunez, 2024).

Medical Research

The other clinical research on these seeds found that it does not support strong evidence that *N. Sativa* has a short-term benefit on dropping systolic and diastolic blood pressure (Albakry et al., 2022). Despite significant use of *N. Sativa* in traditional medicine practices in Africa and Asia, there is inadequate high-quality clinical evidence to indicate that consuming the seeds or oil can be used to treat human diseases.

Nigella sativa contains various compounds, including thymoquinone, which have been shown to perform antioxidant properties. These compounds aid in neutralizing injurious free radicals in the human body, potentially dipping oxidative stress and inflammation. The main active compound in *Nigella sativa*, Thymoquinone, has demonstrated anti-inflammatory effects in several studies. This is useful for conditions categorised by inflammation, such as arthritis, asthma, and certain skin disorders (Toor et al., 2024).

Respiratory Health

Research suggests that *Nigella sativa* may have benefits for respiratory health. It has the potential to assuage symptoms of asthma and allergies, possibly because of its anti-inflammatory and bronchodilator properties.

Diabetes Management

Some studies indicate that *Nigella sativa* may support normalise blood sugar levels and recover insulin sensitivity in persons with diabetes. This could be accredited to its antioxidant properties, as well as its potential to enhance glucose uptake by cells (Toor et al., 2023).

Cardiovascular Health

There is sign to suggest that *Nigella sativa* may have constructive effects on cardiovascular health. It may assist reduce blood pressure and cholesterol levels, dropping the risk of heart disease and stroke (Adinortey et al., 2013). Additionally, its antioxidant properties may protect against oxidative damage to blood vessels.

Anticancer Potential

Thymoquinone has been considered for its potential anticancer effects. Research shows that it may obstruct the development of cancer cells and encourage apoptosis (programmed cell death) in various categories of cancer, counting breast, prostate, colon, and pancreatic cancer. However, more research, including clinical trials, is needed to confirm these findings and determine the optimal use of *Nigella sativa* in cancer treatment (Almatroodi et al., 2020).

Antimicrobial Activity

Nigella sativa has also been considered for its antimicrobial properties. It may have antibacterial, antifungal, and antiviral effects, which could be beneficial for combating infections caused by pathogens.

Treatment for Arthritis

Anti-inflammatory Properties

Nigella sativa comprise of compounds like thymoquinone that have demonstrated anti-inflammatory effects in studies. Inflammation performs a key role in the progression of rheumatoid arthritis, contributing to joint pain and damage (Toor et al., 2023). By reducing inflammation, *Nigella sativa* may help alleviate symptoms associated with RA.

Pain Relief

Some research suggests that *Nigella sativa* may have analgesic properties, meaning it could help relieve pain associated with arthritis. This could improve the quality of life for individuals with rheumatoid arthritis by reducing discomfort and stiffness in the joints.

Antioxidant Activity

Oxidative stress is concerned in the development and progression of rheumatoid arthritis (Albakry et al., 2022). *Nigella sativa's* antioxidants properties may support neutralize free radicals and reduce oxidative damage to joint tissues, potentially slowing the progression of the disease.

Immunomodulatory Effects

Rheumatoid arthritis is an autoimmune condition characterized by an overactive immune response that targets the body's own tissues. Some studies suggest that *Nigella sativa* may have immunomodulatory effects, meaning it could help regulate the immune system and reduce the abnormal immune response seen in RA (Albakry et al., 2022). .

Joint Protection

Nigella sativa may help guard joint tissues from damage triggered by inflammation and oxidative stress. By preserving joint health, it could potentially slow down the progression of rheumatoid arthritis and prevent further deterioration of the joints.

Reduction of Autoimmune Response

Rheumatoid arthritis is followed by an autoimmune response in which the body's immune system erroneously attacks its own tissues, particularly the synovium (lining of the joints) (Darakhshan et al., 2015). Some research suggests that *Nigella sativa* may modulate the immune response, potentially reducing the severity of autoimmune reactions and the associated joint damage.

Combination Therapy

Nigella sativa may complement conventional treatments for rheumatoid arthritis. Some studies have investigated its use alongside conventional medications, such as disease-modifying antirheumatic drugs (DMARDs) and nonsteroidal anti-inflammatory drugs (NSAIDs), to enhance their effectiveness or reduce their side effects (Darakhshan et al., 2015).

Improved Quality of Life

By reducing pain, inflammation, and joint stiffness, *Nigella sativa* could improve the overall quality of life for individuals living with rheumatoid arthritis (Adinortey et al., 2013). Enhanced mobility, decreased reliance on pain medications, and better management of symptoms may contribute to a better sense of well-being and daily functioning.

Potential for Disease Modification

While current treatments for rheumatoid arthritis focus primarily on managing symptoms and slowing disease progression, there is growing interest in therapies that can adapt the course of the disease itself (Mousavi et al., 2024). Some researchers speculate that *Nigella sativa* may have disease-modifying properties, but more evidence is needed to support this claim.

Safety and Tolerability

Nigella sativa is generally considered safe when used in appropriate doses, with few reported side effects. Unlike some conventional medications for rheumatoid arthritis, which may cause gastrointestinal issues, liver toxicity, or other adverse effects, *Nigella sativa* is often well-tolerated. While these potential benefits are promising, more research, particularly clinical trials involving human participants, is needed to fully understand the efficiency of *Nigella sativa* in the treatment of RA (Mousavi et al., 2024). Additionally, it's important to consult with a healthcare professional prior using *Nigella sativa* or any other herbal supplement as a treatment for arthritis, especially if you're already taking medications or have other medical conditions.

Conclusion

Nigella sativa has shown anti-inflammatory, analgesic as well as immunomodulatory and RA lesion reducing effects in studies including in vitro, in vivo and clinical trials. Studies proved the efficiency and safety of *N.sativa* in the rheumatoid arthritis patients by reducing pain and inflammation in the joints of patients. Anti-oxidant properties of N. sativa have also been tested and are shown to be remarkable as it reduces oxidative stress in animal models as well as clinical trials. Research has shown that thymoquinone, the major and active component in Nigella sativa is responsible for its anti-inflammatory, anti-oxidant and analgesic properties. Combination therapy using Nigella sativa with non-steroidal anti-inflammatory drugs or stem cells would be more effective in the treatment of RA. Further in vitro and in vivo studies are needed to confirm the efficacy of nigella sativa against RA.

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