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Role of Aloe Vera in Rhematoid Arthritis

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ABSTRACT

Rheumatoid arthritis (RA) is a chronic autoimmune disorder. It is characterized by persistent synovial inflammation that can have a damaging effect on tissues. Despite its prevalence, RA is still a major cause of disability and lost productivity. One of the major therapeutic targets for the treatment of this autoimmune disease is tumour necrosis factor-alpha (TNF-α).

Aloe Vera is one of the oldest medicinal plants and also considered as wonder plant because of its wide range of properties and uses. It is a main ingredient in many herbal medicines and many cosmetic products that are prepared now days. It has been used externally as well as internally in various disease conditions such as wound, burn, skin problems, spleen enlargement, liver diseases, asthma, jaundice, ulcers, constipation, helps in IBD, gastric and duodenal ulcer, and rheumatoid arthritis. Aloe is the dried juice of the leaves of Aloe barbadensis miller. It belongs to Liliaceae family. It contains many chemical constituents Vitamin A, C and E, enzymes such as carboxypeptidase, cellulase, lipase, alkaline phosphatase, brady kinase, anthraquinone, sugars like Acemannan and glucomannan, organic acid. Hormones like auxin and gibberellin and minerals such as Calcium, Chromium, Magnesium and Zinc. These chemical constituents have anti-arthritic, anti-inflammatory, anti-oxidant, immunomodulatory and analgesic activity which confers its use in the management of rheumatoid arthritis.

In this review paper role of Aloe Vera is elaborated in the management of rheumatoid arthritis.

KEYWORDS-Aloe Vera, Anti-inflammatory, autoimmune disorder, Rheumatoid Arthritis

INTRODUCTION

Rheumatoid arthritis (RA) is the most common chronic form of inflammatory arthritis, affecting approximately 1 percent of the population. It results from complex interactions between genes and environment, leading to a breakdown of immune tolerance and to synovial inflammation in a characteristic symmetric pattern. Distinct mechanisms promote and regulate inflammation and matrix destruction, including damage to bone and cartilage.

Immunomodulation is an important factor for overcoming various acute and chronic infections, especially in the present times when various bacterial species have increasingly become resistant to antibiotics. Taking this into consideration, it has been proved that herbs showing both immunostimulatory and antimicrobial properties might provide useful alternative infections treatment. *Aloe vera* (*Aloe barbadensis*, *Liliaceae*) is a perennial succulent plant in tropical climates. Aloe gel, the colourless substance obtained from the parenchymatous cells in the fresh leaves of *Aloe vera*, contains polysaccharides (pectins, hemicelluloses, glucomannan, acemannan, and other mannose derivatives) and it should not be confused with the laxative drug “Aloe” (bitter yellow exudate containing anthracene glycosides, product of specialized resin canal cells in the thick leaf epidermis). These two products, despite the fact that they share certain components, have distinctly different properties. Traditionally, aloe gel was

mainly used for treatment of inflammatory skin disorders, thermal and radiation burns, arthritis and for wound healing.

Recent studies have shown that aloe vera is considered as a natural treatment for RA. It helps with the relief in joint pain and immunity and enhance mobility.

Aloe Vera is a species of Aloe, native to Northern Africa. It is a stem less or very short stemmed succulent plant growing to 30-36 inches tall, spreading by offsets and root sprouts. Aloe Vera has long been a popular houseplant. Often called the 'miracle plant' or the 'natural healer'.

It flourishes in warm and dry climates, and to many people it looks like a cactus with fleshy thorny leaves. In fact it is a member of the Lily family, staying moist where other plants wither and die by closing its pores to prevent moisture loss. There are over 400 species of Aloe, but it is the Aloe Barbadensis Miller (Aloe Vera or "true Aloe") plant. The 385 species of Aloe is useless and some contain poison. Only few species give useful benefits for health, among these aloe vera is most beneficial species.

Fully grown, the plant stands 30-36 inches high, and a mature leaf is 2.5-3 inches wide at the base, weighing 1.5 to 2 kg.

The Aloe leaf structure is made up of four layers:

1. Rind - the outer protective layer.
2. Sap - a layer of bitter fluid which helps protect the plant from animals.
3. Mucilage Gel - the inner part of the leaf that is filleted out to make Aloe Vera gel.
4. Aloe Vera (inner gel) contains the 8 essential Amino Acids that the human body needs but cannot manufacture.

UNDERSTANDING ALOE AND ITS USES

The Aloe Vera plant contains a gel within it that people have used for centuries for healing purposes. It has external uses as well as internal uses.

External use: Aloe Vera is known to heal skin. Many people will testify that Aloe Vera penetrates their skin rapidly and aids in healing their skin faster than ever thought possible. Aloe Vera is used in this manner in forms of Aloe Vera skin care products. This can be: Aloe Vera lotion, Aloe Vera creams and Aloe Vera gels. People use Aloe Vera skin care products to heal cuts, scrapes and burns.

Pregnant woman has been known to use Aloe Vera lotion and Aloe Vera gel to make stretch marks disappear. People have even been using Aloe Vera to reduce the appearance of scars and wrinkles.

Studies have shown that Aloe Vera helps new skin cells form and hastens healing. The Aloe Vera plant has the amazing ability to provide essential nutrients needed to promote healthy tissue growth by reducing inflammation and killing bacteria and other foreign organisms that thrive on damaged skin cells caused by burns. Aloe Vera's cooling effect offers instant relief from burns and will typically prevent, or greatly reduce, blistering when applied immediately after receiving a burn.

It is reputed to be effective in the treatment of seborrhoea, herpes, red spots, psoriasis, eczema, mycosis and fever blisters. It is proven that the pulp of Aloe Vera relieves the itching due to allergies and insect bites, as well as aiding in the healing, in both man and animals.

The combination of natural ingredients, from 100% pure Aloe Vera and antioxidant vitamins, to marine extracts and chamomile, will protect, nourish and soothe skin. With Aloe Vera cosmetics, you can look beautiful and nourish your skin at the same time. Aloe Vera can also be used as a treatment for many types of skin conditions. It promotes healthy healing of minor cuts, scrapes and scratches. It seals off the injury and helps new skin cells form. Aloe Vera works well for burns, sunburns and even frostbite. It increases

the blood flow to burnt tissue, which greatly quickens the healing of damaged cells. It also has enzymes that relieve pain, reduce inflammation and decrease redness. It even has anti-fungal and antibacterial properties.

Internal Use: Aloe Vera is not just used as Aloe Vera skin care products. Aloe Vera can also be used internally. Many people consume Aloe Vera gel to help with many things. A common thing Aloe Vera gel is used for is constipation. Many people also use Aloe Vera gel to ease the pain or ulcers and arthritis. Not all of the benefits of Aloe Vera ingested internally have been proven scientifically. But people testify that it works for them.

Aloe Vera gel also has many positive healing benefits on your body. An analysis of the Aloe Vera plant has conclusively shown that it is made up of a large variety of substances that are found in the human body; vitamins and minerals, amino acids and enzymes. Perhaps no other plant more closely matches the biochemistry of the human body. Aloe Vera gel acts as a detoxifier and healing agent inside your digestive tract and nearly anyone who has digestive problems may benefit from drinking Aloe Vera gel. Many people have also had great success when taking Aloe Vera gel for ulcers. Aloe Vera gel is not just for people with digestive problems though. Regular daily dosages of Aloe Vera gel will often increase a person's energy level dramatically and gives a feeling of general wellbeing.

Immune System Function: Aloe Vera is full of vitamins, minerals and other nutrients that can help heal stomach and digestive disorders. Research has shown that it balances and modulates the immune system, thereby lowering food intolerances and the body's reaction to them.

Bone protection: Aloe Vera stimulates the activity and proliferation of fibroblasts which in turn significantly increases collagen synthesis. This action is due to the presence of Glucomannan, a mannose-rich polysaccharide, and gibberellin, a growth hormone that interacts with growth factor receptors on the fibroblast thereby stimulates its activity and proliferation. Aloe Vera breaks down the bradykinin as it contains brady kinase enzyme and reduces inflammation. Aloe Vera also act by scavenging superoxide anions, and this activity have seen attributed to the caffeoyl group of isorabaichromone, a derivative of aloe sin.

Anti-inflammatory activity: Aloe vera shows promise for rheumatoid arthritis (RA) due to its anti-inflammatory compounds that target pain-inducing substances and cytokines like TNF-α, potentially reducing joint inflammation and swelling, with research exploring topical gel, oral juice, and specific compounds like aloesin for broader therapeutic effects, though more clinical trials are needed. Most recent studies on anti-inflammatory activity of *Aloe vera* are focused on the action mechanism of isolated compounds in murine macrophage RAW264.7 cells and mice stimulated with LPS. Hence, the potential anti-inflammatory effect of aloin is related to its ability to inhibit cytokines, ROS production, and JAK1-STAT1/3 signalling pathway. Moreover, aloe-emodin sulphates/glucuronides (0.5 μM), rhein sulfates/glucuronides (1.0 μM), aloe-emodin (0.1 μM), and rhein (0.3 μM) inhibited pro-inflammatory cytokines and nitric oxide production, iNOS expression, and MAPKs phosphorylation.

In another study, Thunyakitpisal et al. demonstrated that acemannan increased IL-6 and IL-8 expression and NF-κB/DNA binding in human gingival fibroblast via a toll-like receptor signaling pathway. Since there is a relation between high IL-1β levels and periodontal diseases, Na et al. investigated the anti-inflammatory properties of aloin in human oral KB epithelial cells stimulated with saliva from healthy volunteers. This study revealed that those saliva samples with high content in IL-1β stimulated IL-8 production in KB cells, and pretreatments with aloin inhibited IL-8 production by decreasing p38 and extracellular signal-regulated kinases pathway.

With all of the benefits that are known for Aloe Vera, it is no wonder people use Aloe Vera so much. Many preparations are available that claim to provide Aloe Vera in tablet or capsule form. It is unlikely that many of the delicate beneficial components will survive the manufacturing process, and these products often contain so little Aloe Vera anyway. The market for Aloe Vera products is so clouded with conflicting claims with manufacturers in for a quick buck, and unscrupulous players, that it is no wonder that many health professionals remain sceptical of the benefits of Aloe Vera.

ALOE CONSTITUENTS

Aloe vera is considered as a boon for Rheumatoid Arthritis. The constituents present in aloe vera manages the immunity and helps in the mobility.

Aloe vera's anti-rheumatic properties come from a complex mix of constituents like polysaccharides (Acemannan), anthraquinones (aloin, emodin), vitamins (A, C, E), enzymes (bradykinase), minerals, and fatty acids, working synergistically to reduce inflammation, pain, and oxidative stress, by inhibiting pro-inflammatory mediators like TNF-α and prostaglandins, making it a promising natural aid for Rheumatoid Arthritis (RA) management.

These properties can help reduce pain and inflammation in affected joints.

PATHOGENESIS OF RA

Rheumatoid Arthritis (RA) pathogenesis is a complex autoimmune process where genetic predispositions (like HLA-DRB1) interact with environmental triggers (like smoking, infections) to initiate an immune response, often starting at mucosal sites (lungs, gut). This leads to the production of autoantibodies (ACPA) and the activation of T and B cells, resulting in chronic inflammation, cytokine release, immune cell infiltration (macrophages, lymphocytes) into the synovium, and the formation of destructive pannus tissue that damages cartilage and bone.

Small-molecule mediators of inflammation, autoantibodies, cytokines, growth factors, chemokines, and matrix metalloproteinases (MMPs) subsequently contribute to the initiation and perpetuation of arthritis. Synovial inflammation also activates mesenchymal cells in the joint that can exhibit aggressive behaviour and can invade and destroy cartilage while osteoclasts damage subchondral bone. Irreversible loss of articular cartilage and bone begins soon after the onset of RA, and early interventions can improve long-term outcomes.

MECHANISM OF ACTION OF ALOE IN RA

Aloe vera helps manage Rheumatoid Arthritis (RA) by reducing inflammation through inhibiting pro-inflammatory cytokines (like TNF-α, IL-6), suppressing inflammatory pathways (COX/LOX), reducing oxidative stress with antioxidants, and calming mast cells, all while promoting healing and potentially modulating immune cell activity via compounds like aloesin and polysaccharides, thereby easing pain and swelling.

The cytokines IL-1 and TNF play an important role by stimulating the cells of pannus to produce collagenase and other neutral proteases that contributes to local demineralization of bone by activating osteoclasts that accumulate at the site of local bone resorption and Aloe barbadensis mediates its action by decreasing the level of these cytokine -TNF and IL-1 in plasma.

The production of large amounts of cyclo-oxygenase and lipo-oxygenase pathway products of arachidonic acid metabolism by cells in the synovial fluid and tissue further aggravates the inflammation and Aloe

Vera and also act by inhibiting COX- pathway and reduces the production of prostaglandin E2. Polymorphonuclear leukocytes can ingest the immune complexes, with the resultant production of reactive oxygen metabolites and Aloe barbadensis act through the alteration of primary and secondary metabolites via salicylic acid elicitation.

Pro-inflammatory cytokines tumour necrosis factor and the reactive free radical nitric oxide (NO) synthesised by Inducible NO Synthase (iNOS), aloe-emodin inhibited inducible nitric oxide synthase (iNOS), mRNA expression and nitric oxide (NO) production.

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PHARMACOLOGICAL ACTIVITY

Robbers et al.1996, reported presence of amino acid which are essential in wound healing process are present in Aloe Vera.

Bozzi et al.2007 reported that it also contains many inorganic electrolytes like iron, potassium, magnesium, chromium, copper, sodium, calcium and zinc which are vital part of wound healing process. It stimulates the body to produce antibodies and starts wound healing by releasing growth factors.

In 1989, Davis et al. demonstrated the anti-inflammatory activity of Aloe Vera in diabetic mice, and in another study 1% carrageenan were used to induce inflammation similar to arthritis and reduction of vascularity of carrageenan inflamed synovial pouches by 50% after treatment with 10% Aloe barbadensis indicated the anti-inflammatory activity which was further strongly supported when number of mast cell was decreased by 48% compared to only 1% in carrageenan-treated mice. Finally, the increased number of fibroblasts strongly demonstrated that Aloe barbadensis stimulates fibroblasts to grow and repair.

A study done by Radha and Laxmipriya 2015 exhibits strong anti-inflammatory effects due to the presence of anthraquinones and chromone.

Aburjai and Natsheh, 2003; Eshun and He, 2004; Radha and Laxmipriya, 2015 reported that a number of antioxidants such as α-tocopherol, carotenoids, ascorbic acid, flavonoids, tannins, vitamin C and E are present in Aloe Vera.

Lopez et al 2013 reveal antioxidant potential of the extracts of Aloe Vera.

Kang et al ,2014 investigated the antioxidant potential of a polysaccharide isolated from Aloe Vera gel, showed that it had a protective effect against dihydrochloride induced oxidative stress and cell death in kidney epithelial cells.

CONCLUSION

This work was designed to evaluate the potential role the selected major components present in *Aloe vera* in the management of RA and its symptoms through inhibition of the pro-inflammatory cytokine TNF-α.

Aloe Vera is widely used in various disease conditions specially in skin diseases but it also plays a remarkable role in the management of rheumatoid arthritis. It is also mentioned in classical literatures that

it possesses Moḥallil-i Waram (Anti-inflammatory) properties and modern scientific research on animals has also confirmed its anti-inflammatory, anti-oxidant, analgesic and immuno-modulatory activity. Therefore, it can be concluded that Aloe Vera is effective in the management of Rheumatoid arthritis.

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