The immunosuppressive effect of boswellic acid in managing the inflammation and symptoms associated with psoriatic arthritis

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KEYWORDS
Auto-immune, psoriasis, anti-arthritic, boswellic acids.

ABSTRACT:
*Psoriatic arthritis (PsA) is a long-term inflammatory autoimmune condition that affects the skin and joints. It is associated with psoriasis, a skin disorder that causes red, scaly patches. If neglected, PsA can result in gradual joint deterioration, stiffness, oedema, and joint discomfort. In 30% of cases, psoriatic arthritis (PsA), a complicated inflammatory illness with varied clinical manifestations, exacerbates psoriasis. In addition to preventing outbreaks and slowing the course of PsA, current medical treatment methods can also aid people with their symptoms by using natural and alternative therapies. There is various herbal product used in the treatment management of PsA in which Indian frankincense (Boswellia serrata) can be used as an alternate option for the management of inflammation and symptoms associated with PsA. The literature searched for reports of B. serrata and isolated BAs having anti-cancer, anti-microbial, anti-inflammatory, anti-arthritic, hypolipidemic, immunomodulatory, anti-diabetic, hepatoprotective, anti-asthmatic, and clastogenic activities. Boswellia serrata has a key active ingredient, Boswellic acids which shows potential for use in the treatment of **psoriatic arthritis (PsA)** due to its strong anti-inflammatory and immune-modulating properties.Studies have shown significant improvements in joint pain, stiffness, and swelling with boswellic acid supplementation. Although specific studies on PsA are limited, the mechanisms of boswellic acid suggest its efficacy in reducing both joint and skin symptoms due to shared inflammatory pathways with other forms of arthritis.*

1. Introduction

Psoriatic arthritis (PsA) is a chronic, inflammatory, musculoskeletal disease that is linked to psoriasis. Up to 30% of patients with psoriasis may develop PsA over the course of their lifetime. Musculoskeletal manifestations of PsA include peripheral arthritis, spondylitis, dactylitis (inflammation of the whole digit) and enthesitis (inflammation where a tendon, ligament or joint capsule inserts onto the bone) (Alexis Ogdie 2020).Patients with PsA have physical function limits, fatigue, sleep disturbances, decreased job capacity, and decreased social involvement in addition to their musculoskeletal and skin characteristics. PsA is linked to a number of comorbidities, such as obesity and metabolic disease (diabetes, hypertension, hyperlipidemia, fatty liver disease, cardiovascular outcomes), depression, and anxiety, in addition to extra-articular manifestations like uveitis and inflammatory bowel disease (IBD). (AnaBelén Azuaga 2023)

In the past, PsA was thought to be a quite harmless illness. Nevertheless, it is now generally accepted that PsA has a functional impact that is similar to that of other inflammatory arthritis types, such as axial SpA (axSpA) and rheumatoid arthritis (RA). There are gradual and damaging alterations that are indicative of PsA in many people. In the early stages of PsA, significant pathological alterations already take place, and within two years of the illness initiation, almost half of the patients exhibit structural damage.(Sonia Sundanum 2023)

1. Pathogenesis of PsA

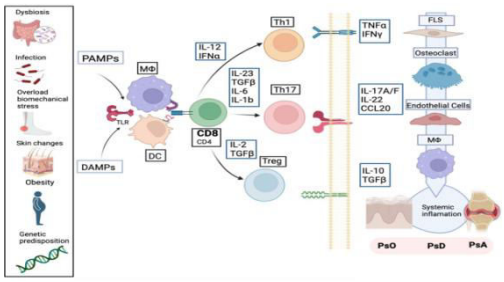

Figure 1. Pathological processes in psoriatic disease (PsD). Predisposing genetic background, infections, obesity, or biomechanical factors act as triggers and precipitate disease onset by activating DC macrophages which present antigens through type major histocompatibility complex (MHC) I to Tcells (mainly CD8), through Toll-like receptor (TLR) type 2. This favors the local release of cytokines by triggering the innate and adaptive immune response. IL-12 and IFNα stimulate the Th1 response, which releases TNFα and IFN-γ. IL-23, TGFß, IL-6, and IL-1b activate the Th17 response in the presence of IL23, leading to the release of IL17 (mainly A isoform), IL22, IL26, and CCL20. Moreover, regulating and deactivating the inflammatory cascade requires the response mediated by Treg cells through IL-2 and TGFß. These released cytokines interact with their transmembrane receptor promoting the release of more cytokines and attracting endothelial cells, macrophages, fibroblasts, keratinocytes, dendritic cells, epithelial cells, chondrocytes, osteoclasts, and osteoblasts. Activation of the immune system leads to synovitis, enthesitis, erosions, and lesions in the articular cartilage and skin. DAMPS (Damage-associated molecular pattern), PAMPs (Pathogen-associated molecular patterns), DC (dendritic cells), MΦ (Macrophages), CD8 (CD8 T lymphocyte), CD4 (CD4 T lymphocyte), Th1 (T helper 1 cells), Th17 (T helper 17 cells), Treg (T regulatory), FLS (synovial fibroblast). (AnaBelén Azuaga 2023)

Although the exact origin of PsA is unknown, a complex interaction of immunological, genetic, and environmental variables is thought to be responsible. Specific human leukocyte antigen (HLA) alleles, namely HLA-B*27, HLA-B*08, HLA-B*38, and HLA-B*39, exhibit a strong correlation with the prevalence of PsA. These genotypes are thought to alter the immune response to self-antigens, making people more vulnerable to PsA. Additionally, in those with a genetic susceptibility, environmental events like as infections and mechanical stress may serve as catalysts for the development of PsA. The development of PsA may be influenced by the gut and skin microbiomes. The pathophysiology of PsA is thought to be significantly influenced by immunological variables, such as cytokines and chemokines. The inflammatory response, tissue damage, and bone erosion linked to PsA have been identified as being significantly influenced by tumor necrosis factor-alpha (TNF-), interleukin-17 (IL-17), and interleukin-23 (IL-23). The degree of this involvement of the skin, enthesis, and synovium may vary among individuals and is influenced by immunology, genetic and environmental factors. (Bong-Woo Lee 2023)

2.1. Immunopathology

PsA is initiated by the stimulation of dendritic cells (DCs) and macrophages.Major Histocompatibility Complex (MHC) I facilitates the toll-like receptor-2 (TLR-2) signaling pathway, which is how these cells present antigens to T lymphocytes.Thus, a variety of cytokines, including IL-1, IL-6, TNF-α, IL-17, and IL-23, are secreted in greater amounts when both innate and adaptive immune responses are activated. Furthermore, it is thought that the start of inflammatory and damaging processes in the joints depends on the activation and invasion of T cells and macrophages.

In particular, DCs present antigens and release a variety of pro-inflammatory cytokines to stimulate T cell development. TLR-2 expression has been found to be elevated in PsA patients' immature DCs. In their synovial fluid, patients with PsA had a higher percentage of immature myeloid DCs than plasmacytoid DCs. TLR activation causes T cells in PsA to polarize toward the Th1 subgroup, which in turn increases the production of TNF, IFN-α, and IL-2. Cytokines such as IFN-α, TNF-α, IL-12, and IL-23 are produced by plasmacytoid DCs and act as cues for CD4+ and CD8+ T cell clonal growth. Interferon, IL-2, IL-4 TNF, and interleukin (IL)-17A are T cell response cytokines that are present in both the synovial fluid and the inflamed synovium, demonstrating the crucial role that T cells play in the immunopathogenesis of PsA. The focus has

switched considerably over the past ten years from TNF and Th1 response cytokines to Th17 cells, IL-23, and IL-17 as studies have identified important drivers of illness in PsA. These goals have received approval from international regulatory bodies and have shown relevance in randomized controlled trials (RCTs).

IL-12 is increased upon introduction of an antigen to the first T cell. Th1 cell development and proliferation follow, which leads to the production of pro-inflammatory cytokines including TNF. However, it is believed that IL-23 initiates Th17 cell differentiation. Thus, IL-22 and IL-17 are released, which causes TNF to be upregulated.In the synovium of PsA patients, there are many B lymphocyte aggregates. It is unclear, therefore, if B-cells play a part in the development and progression of disease. Interestingly, there is no evidence linking PsA to autoantibodies in circulation. Furthermore, there is only a slight benefit to using monoclonal antibodies that target CD20 expressed on B cells to treat PsA. Though it differs from the synovium in RA, the synovial tissue in PsA is comparable to that seen in other spondyloarthritis (SpA). Synovial macroscopic analysis in PsA shows a markedly different vascular pattern with possibly significant pathogenic consequences when compared to RA.

Activated macrophages take part in a number of synovial pro-inflammatory activities. Patients with PsA who responded to treatment showed a decrease in the number of CD68+ macrophages in their synovium, highlighting the significance in the pathophysiology of PsA. In animal models, skin inflammation brought on by a TLR-7 ligand was linked to CD68+ macrophage infiltration and increased production of inflammatory cytokines in the joints. According to this study, macrophages may play a key role in the shift from skin to joint inflammation and may also contribute to the inflammatory process in PsA. Angiogenesis, neutrophil recruitment, and synovial fibroblast proliferation are all induced by mast cells found in the synovium, suggesting that these cells may play an active role in inflammatory arthritis. While a limited number of IL-17-positive T cells were found in the synovium of peripheral SpA, mast cells constitute the main source of IL-17A. Similarly, tissue-resident mast cells that produce IL-17A may exacerbate inflammation. However, a more thorough understanding of how mast cell release of IL-17A is regulated in the inflammatory tissue is still pending.

Innate immune cells have a role in the formation of PsA by generating IL-12 and IL-23, which promote T cell differentiation into two separate subtypes known as Th1 and Th17 helper T cells. This results in the release of IL-22 and IL-17, which raise TNFα-secretion. The increase of CD4+ T17 cells, which release IL-23 and IL-17, in peripheral blood and synovial fluid indicates that T cells are the main cause of PsA pathogenesis. Additionally, PsA patients' afflicted joints showed an abundance of IL-17-producing cells, which may possibly include CD8+ T cells that secrete IL-17. During a study I was found out an increase in the quantity of memory CD8+ T cells within the synovial fluid, surpassing their levels detected in the peripheral blood. Additionally, these cells were identified as active CD8+ T cells expressing the CXCR3 receptor.Furthermore, the synovial fluid was shown to include higher concentrations of CXCR3 receptor ligands, including CXCL9 and CXCL10. It has been established that Th1, Th17, and CD8+ cytotoxic T cells play a significant role in the inflammatory processes in PsA, indicating the presence of unique immune cellular pathways in this illness. Regulatory T cells, or Tregs, are generally believed to have a role in establishing an anti-inflammatory response and inhibiting chronic inflammation.

In conclusion, cytokines including IL-23, TNF-, IL-17 (mostly IL-17A isoform), and IL-22 are produced as a result of interactions between different immune cell types. These cytokines excite tissue-resident cells in the joint and enthesis and cause inflammation. These cells, which include fibroblast-like synoviocytes, chondrocytes, osteoblasts, and osteoclasts, secrete enzymes that break down extracellular matrix and the receptor activator of nuclear factors' B ligand (RANKL), which leads to cartilage degradation, bone erosion, and joint loss. Additionally, when stimulated, these cells release pro-inflammatory mediators to draw in more immune cells and create a long-lasting immunological response in PsA patients. (Bong-Woo Lee 2023)

2.2. Genetics

There is a significant heritability component to PsA, particularly in comparison to RA. Compared to the general population, first-degree relatives had a recurrence risk ratio of over 27, which is significantly greater than the recurrence risk ratio for RA or psoriasis. Psoriasis and PsA susceptibility are linked to class I major histocompatibility complex (MHC) alleles. In contrast, RA is associated with class II MHC alleles. There are variations in the particular genetic predisposition linked to the "psoriatic spectrum." For instance, HLA-C*06 confers susceptibility to psoriasis but not to PsA, according to cross-sectional research.Additionally, several

"sub-phenotypes" of HLA-B*08, B*27, B*38, and B*39, including symmetric or asymmetric sacroiliitis, enthesitis, dactylitis, and synovitis, are linked to specific subtypes of these alleles. Despite these well-established genetic correlations with sub-phenotypes, genotyping has not been found to play a part in patient therapy selection. (Sonia Sundanum 2023)

The short arm of chromosome 6's major histocompatibility complex (MHC) contains many human leukocyte antigen (HLA) alleles or haplotypes.

Hereditary factors play a significant role in psoriatic arthritis and PsO. First-degree relatives (FDR) are present in approximately 7.7% of PsA and 17.7% of PsO. According to a study that used a mixed model approach to evaluate the impact of single nucleotide polymorphisms (SNP) from genomic wide association studies (GWAS), PsO and PsA both have a considerable hereditary burden, albeit a greater one in PsO than in PsA. HLA-B*27, HLA-B*39, HLA-B*38, and HLA-B*08are associated with the risk of PsA, but HLA-B*27 and HLA-B*39 is also associated with a shorter time between PsO and PsA onset. Other genotype the genetic region of the major histocompatibility complex (MHC) in the short arm of chromosome 6 contains several alleles or haplotypes of human leukocyte antigen (HLA) class I that are associated with an increased risk for PsO and PsA and are also associated with several clinical phenotypes of the disease. The HLA-C*06:02 association with PsO is stronger than with PsA and this allele is also associated with an early onset of PsO and a longer time between the onset of skin and joint involvement. HLA-B*27, phenotype associations are: HLA B*08.01 with asymmetric sacroiliitis, peripheral arthritis, ankylosis and increased joint damage, whereas HLAB*27 is associated with symmetric sacroiliitis, dactylitis, and enthesitis. Fine mapping of the MHC region showed that the risk heterogeneity between PsA and PsO might be driven by HLA-B amino acid at position 45, specifically glutamic acid (Glu), which is present in classical HL-B alleles associated with PsA. (Vanessa Ocampo D 2019)

2.3. Environment

There is a great deal of study being done on how environmental factors can induce PsA in genetically sensitive people. Risk factors for the start of PsA have been proposed to include environmental factors including trauma (Koebner's phenomena), infections, smoking, and immunological triggers (such rubella vaccine).

Pathological force levels indicate a biological (mechanical) stress that triggers a tissue repair pathway in tendons and ligaments mediated by the immune system. In addition to its long-established function in "overuse" injuries like tendinopathy, mechanical stress is now being recognized as a potential cause of psoriatic arthritis and other types of chronic inflammatory arthritis. (Sonia Sundanum 2023)

Cytokine	Main Source	Function in PsA
TNF-α	Macrophages, T cells, NK cells, mast cells	Elevation in the levels of cytokines, chemokines, matrix metalloproteinases, and adhesion molecules from various immune cells Induction of osteoclasts to promote the degradation of cartilage and bone
IL-23	Dendritic cells, macrophages	Promotion of Th17 cell differentiation and GM-CSF production
IL-12	Dendritic cells, macrophages	Promotion of Th1 cell differentiation through STAT4
IL-17A/F	Th17 cells, NK cells, type 3 innate lymphoid cells	Stimulation of fibroblast-like synoviocytes, chondrocytes, and osteoclasts Elevation in the levels of pro-inflammatory cytokines and matrix metalloproteinases Induction of neutrophil recruitment
IL-21	T cells, NK cells	Promotion of T cell differentiation (specifically, into Th17 cells)
IL-22	T cells, innate lymphoid cells	Activation of fibroblast-like synoviocytes Promotion of osteoclast and bone degradation
IL-32	NK cells, T cells, monocytes, epithelial cells	Potentiation of inflammation through the activation of NF-κB signaling and promotion of osteoclast differentiation
IL-33	Macrophages, dendritic cells, mast cells, epithelial cells	Activation of Th1/Th17-mediated inflammation
IFN γ	Th1 cells, type 1 innate lymphoid cells, NK cells	Activation of macrophage and T cell Promotion of RANKL secretion
GM-CSF	Macrophages, T cells, synovial fibroblasts	Recruitment of various immune cells
IL-9	Th9 cells	Promotion of Th17-associated inflammation and IL-17A production
IL-6	Macrophages, T cells, endothelial cells	Stimulation of STAT3 signaling to increase the production of pro-inflammatory cytokines
IL-15	Macrophages	Promotion of T cell proliferation; natural killer cell activation; and production of IFN-γ, TNF-α, and IL-17
IL-1α	Macrophages, dendritic cells	Induction of IL-17, IL-21, and IL-22 expression by γδT cells in combination with IL-23

Table 1. inflammatory cytokines in PsA

2. Natural sources for PsA treatment

There are many plants and their bioactive compounds have been traditionally and scientifically explored for their potential in managing **psoriatic arthritis (PsA)**, these plants often have **anti-inflammatory**, **antioxidant**, and **immunomodulatory** properties, which can help alleviate joint pain, reduce inflammation, and improve skin symptoms associated with PsA. Although these plants may not be the first line drugs, but can be used as the alternate drugs in treatment of the symptoms and anti-inflammatory effects. These are:

- Boswellia serrata (Indian Frankincense)
  Active constituents: Boswellic acids, particularly acetyl-11-keto-β-boswellic acid (AKBA).
- Curcuma longa (Turmeric)
  Active constituents: curcumin
- Zingiber officinale (Ginger)
  Active constituents: Gingerols and shogaols.
- Aloe vera
  Active constituent: Polysaccharides, vitamins, and antioxidants.
- Withaniasomnifera (Ashwagandha)
  Active constituents: Withanolides
- Camellia sinensis (Green Tea)
  Active constituents: Epigallocatechin gallate (EGCG).
- Nigella sativa (Black Seed)
  Active constituents: Thymoquinone
- Tripterygium wilfordii (Thunder God Vine)
  Active constituents: Triptolide
- Panax ginseng
  Active constituents: Ginsenosides
- Salix alba (White Willow Bark)
  Active constituents: Salicin (precursor to salicylic acid).

And many more plants can be used but point to be noted that these plant extracts are used as an alternative to treatment of symptoms PsA.(Omali Y. Elkhawaga 2023)

3. Boswellic acids

Boswellia serrata (BS) and other Boswellia species' oleogum resin, also known as frankincense or olibanum, has gained popularity in some European countries over the past ten years as a treatment for a number of chronic inflammatory conditions, such as rheumatoid arthritis, chronic bowel disorders, bronchial asthma, peritumoral brain oedema, and others.Because it can stimulate blood circulation to reduce pain, relax tendons, and encourage detumescence, frankincense is frequently used in traditional Chinese medicine in China to treat osteoarthritis, rheumatism, rheumatoid arthritis, and bruising. (Ammon 2006)

The olive plant Boswellia serrata exudes frankincense, a hard, gelatinous resin. Resin, gum, and volatile oil are the three primary categories into which the complex and varied chemical components of frankincense fall.Boswellia serrata, also known as Salai or Salai guggul, is a moderate to big branching tree that grows in arid mountainous areas of the Middle East, Northern Africa, and India. It belongs to the Burseraceae family. With 600 species scattered across all tropical regions and 17 genera, the Burseraceae family is well-represented in the plant kingdom. The genus Boswellia has roughly 25 species, the majority of which are found in Arabia, the northeastern coast of Africa, and India. Boswellia serrata is mostly sourced commercially from Andhra Pradesh, Gujarat, Madhya Pradesh, Jharkhand, and Chhattisgarh in India. It also goes by several names in different regions. A plant exudate belonging to the genus Boswellia (Family: Burseraceae), salai is an oleo gum-resin. After being tapped from the tree's trunk incision, it is kept in a bamboo basket that has been specially built for that purpose. For around a month, the semi-solid gum resin is left in the basket, allowing its fluid content, known locally as "ras," to continue to seep out. The gum-resin residue, which is semi-solid to solid, gradually solidifies into amorphous, tear-shaped products that have a pleasant aroma. (Siddiqui 2011)

Three of these species have long been regarded as "authentic Frankincense-producing trees."The oleo gum-resins are composed of 30–60% resin, 5–10% essential oils that dissolve in organic solvents, and the remaining ~65% water-soluble polysaccharides (galactose, xylose, and arabinose). Because essential oils are present, the resins have a pleasant scent, which explains their commercial significance. (Ehab A. Ragab 2024)
Composition of BAs: The resinous part of Boswellia serrata contains, monoterpenes (α-thujene); diterpenes (macrocyclic diterpenoids such as incensole, incensole oxide, iso-incensole oxide, a diterpene alcohol [serratol]); triterpenes (such as α- and β-amyrins); pentacyclic triterpenic acids (boswellic acids); tetracyclic triterpenic acids (tirucall-8,24-dien-21-oic acids).
Pentacyclic and tetracycline triterpenes are found in the resins of Boswellia species. Of these, certain boswellic acids (BA) are primarily responsible for many of the pharmacological effects. Tetracycline triterpenic acids are also present, and tirucallic acid has been demonstrated to be pharmacologically active. (Ammon 2006)
Since ancient times, boswellic acid (BAs) has been used as a therapeutic and medicinal substance. It is derived from olibanum or frankincense. Chemically, BAs are connected to pentacyclic triterpenoids that are members of the Olean and Ursane classes.
Acetyl-11-keto-β-BA (AKBA) and 11-keto-β-BA (KBA), two BA derivatives found in plants in the genus Boswellia, are linked to their anti-inflammatory qualities. This review provides a more thorough analysis of BA and numerous Boswellia species and their BA and its derivatives, including their origins, chemistry, synthetic derivatives, pyrolysate products, pharmacokinetics, and biological activities. (Yuqing Gong 2022)

4. Chemistry of BAs

Numerous pentacyclic triterpenic acid derivatives, referred to as BAs, are found in the resin portion of oleogum resin from different Boswellia species. These derivatives are chemically linked to 3-hydroxyolean-12-ene-23-oic acid (α-BA) and 3-hydroxyurs-12-ene-23-oic acid (β-BA). The most potent ingredient thought to be in charge of frankincense's therapeutic effects is BAs. The main BAs and their derivatives which have been isolated from various Boswellia species (particularly B. serrata, B. carteri, and B. sacra) included α-BA, β-BA, acetyl-α-BA (AαBA), acetyl-β-BA (Aβ-BA), 11-keto-β-BA (KBA), AKBA, as well as and 11α-ethoxy-β-BA. In addition to diene derivatives, namely 9,11-dehydro-α-BA, 9,11-dehydro-β-BA [9], acetyl-9,11-dehydro-α-BA, acetyl-9,11-dehydro-β-BA which is believed to originate from their corresponding 11-hydroxyBA. Further BA derivatives have been isolated from acidic and neutral fractions of the gum extract and identified as 2,3-dihydroxy-urs-12-ene-24-oic acid and urs-12-ene 3-α,24-diol, and its isomer urs-12-ene-3-β,24-diol.
There have been reports of certain physical, chemical, and spectral characteristics of the primary BAs and their derivatives that are found in significant quantities in several Boswellia species. It was found that the C-3 hydroxyl and C-24 carboxyl groups in BA had an axially orientated structure. The 11-keto group in BA must fit with the receptors in order to produce anti-inflammatory activity; if the group is substituted with a methylene group, reduced to alcohol, or deacetylated in 3-acetyl 11-keto derivatives, the activity will be reduced. BA with a smaller 11-keto group was more successful in inhibiting topoisomerase enzymes and causing apoptosis. (Ehab A. Ragab 2024)

5. Pharmacokinetics of BAS

Any drug's therapeutic action and dose form determination are generally determined by its bioavailability, which is reliant on absorption. Because of their lipophilicity, particularly KBA and AKBA, and extensive metabolism, BA and its derivatives have low absorption, which limits their systemic bioavailability and results in minimal therapeutic effects. While acetylated BA compounds are resistant, non-acetylated BA derivatives are extensively metabolized in the liver during phase I, producing hydroxylated derivatives. After oral treatment, both KBA and AKBA are poorly absorbed; however, AKBA is more widely distributed in brain cells and has a stable metabolism than KBA, which has significant phase I metabolism and is widely dispersed in plasma.
According to certain research, fatty meals should be had every six hours in order to maximize the plasma levels of BAs.

The pharmacokinetics, bioavailability, and absorption of BAs can all be impacted by food consumption, which can also impact the drugs' therapeutic and medical effects.

By combining BA and its derivatives with anionic medications, structured meals, or nanoemulsion, its restricted bioavailability can be increased. (ammon 2016)

6. Mechanism of action of BAs (AKBA)

Boswellic acids work by reducing inflammation in the skin and joints, which are key components of psoriatic arthritis (PsA), by focusing on particular inflammatory pathways. Acetyl-11-keto-β-boswellic acid (AKBA) from frankincense extract has a range of pharmacological properties, such as anti-inflammatory, anti-infection, anti-tumor, antioxidant, and anti-aging effects. Numerous signaling pathways, including the NF-κB, Nrf2/HO-1, and ERK pathways, have been demonstrated to be modulated by AKBA. Important enzymes in the manufacture of leukotrienes, including 5-lipoxygenase (5-LOX), leukocyte esterase, and TNF-α, can also be inhibited by AKBA. By preventing the formation of biofilms, AKBA offers resistance to bacterial infection. It has also been shown to be effective against the SARS-CoV-2 virus by binding to its functional proteins.

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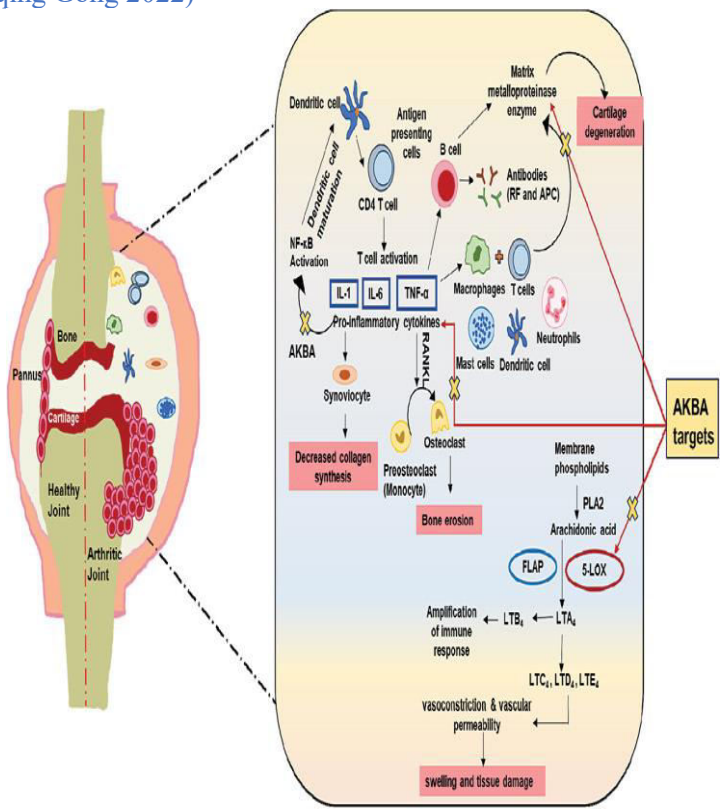

Figure 2: signalling pathway and molecular targets modulated by AKBA in arthritis

Key mechanisms include:

i.Inhibition of 5-Lipoxygenase (5-LOX) Pathway

- Boswellic acids prevent leukotrienes from being produced by inhibiting the 5-lipoxygenase (5-LOX) enzyme.Leukotrienes are pro-inflammatory mediators that contribute to joint inflammation, enthesitis, and dactylitis in PsA.

ii.Suppression of Pro-inflammatory Cytokines

- Boswellic acids suppress the production of cytokines involved in PsA's pathogenesis, including:
- TNF-**α** (Tumor Necrosis Factor-alpha)
- IL-**1β** (Interleukin-1 beta)
- IL-**6** (Interleukin-6)
- IL-**17** and **IL-23**, critical components of the **Th17/IL-23 axis**, which drive inflammation in PsA.

iii.Regulation of Immune Cells

- It modulates the activity of:
- T **helper cells (Th17 cells)**, which produce IL-17, a key cytokine in PsA.
- Macrophages **and neutrophils**, reducing their recruitment and activation in inflamed tissues.

iv.Inhibition of Matrix Metalloproteinases (MMPs)

- Boswellic acids inhibit MMPs, which are enzymes that break down cartilage and extracellular matrix components in PsA-affected joints.

v.Antioxidant Activity

- Reduces oxidative stress by scavenging free radicals and inhibiting reactive oxygen species (ROS).

vi.Reduction of NF-κB Activity

- Boswellic acids inhibit **NF-κB**, a transcription factor that regulates the expression of many pro-inflammatory cytokines and enzymes.

7. Conclusion

From this review, it has become clear that AKBA is a good alternate option in treating symptoms of PsA. PsA is an arthritis that is associated with psoriasis. AKBA has wide range of pharmacological actions against many chronic diseases. They can attack multiple mechanisms that contribute to disease progression. Numerous chronic diseases owe a great deal to the actions of NF-B, MAPK, Erk-1/2, TNF-α, etc., all of which were found to be affected by BA treatment. It improves psoriatic skin lesions and alleviates joint pain, stiffness and swelling. It can be given in forms of capsules, topical preparations and even directly as extracts. Topical application of anti-inflammatory molecules is a feasible alternative to systemic approaches to treat psoriatic and eczematous symptoms by directly acting on inflammatory processes and generating a marked soothing response in skin.

Conflict of interest : None

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