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ROLE OF FENOPROFEN AND OTHER THERAPEUTIC AGENTS IN MITIGATION OF INFLAMMATORY ARTHRITIS: ADVANCEMENT AND TREATMENT STRATEGIES

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Abstract: Disabling conditions associated with inflammatory arthritis are common among the elderly. Joint pain, decreased function, and a lower quality of life are all results of degenerative joint diseases such osteoarthritis (OA) and rheumatoid arthritis (RA). Inflammatory arthritis can be treated in a variety of ways, including with anti-inflammatory drugs given through oral, topical, or intra-articular methods, surgical intervention, and physical therapy. Because of the overwhelming cost and minimal therapeutic efficacy, developing novel alternative techniques to controlling inflammatory arthritis has remained the big challenge. Fenoprofen is an anti-inflammatory drug used to treat inflammatory conditions such gout, osteoarthritis, rheumatoid arthritis, and degenerative joint disease. It works as well as other nonsteroidal anti-inflammatory medicines, if not better. In the medical field, calcium salt is employed for the treatment of mild to moderate pain, as well as the alleviation of inflammatory conditions like arthritis. Platelet aggregation can be temporarily slowed by fenoprofen. This session discusses the history of fenoprofen's use in the treatment of arthritis, as well as the current state of the art in the use of alternative therapeutic agents to combat the condition. Phytocompounds have been studied, and some compounds have been proven to have anti-arthritic potential, which could help alleviate the problems caused by these therapies, such as side effects and high costs. The efficacy of some complementary and alternative medicine practices, such as yoga, acupuncture, massage therapy, and tai chi, in the management of arthritis has also been demonstrated.

Keywords: Inflammatory arthritis, fenoprofen, NSAIDs, DMARDs, prostaglandins

Introduction:

The symptoms of inflammatory arthritis (IA) include morning stiffness that lasts for an hour, joint pain, swelling, warmth, and tenderness in the joints, and generalized joint discomfort [1]. It falls under the umbrella term "arthritis," which includes both inflammatory and non-inflammatory forms. The first stage in diagnosing and treating a patient with arthritis is determining whether the patient is experiencing inflammatory or non-inflammatory symptoms [2]. It is anticipated that the number of cases of arthritis detected by medical professionals will rise during the next few decades. In 2040, it is predicted that 78.4 million adults aged 18 and above will have arthritis, up from the expected 58.5 million adults in 2016-2018 (23.7%) [3]. Most kinds of inflammatory arthritis are systemic, thus other signs of inflammation, such as rashes, eye inflammation, hair loss, dry mouth, and fever, can occur anywhere in the body [4,5]. More cells and inflammatory substances within the joint can irritate it, leading to cartilage breakdown and synovial edema [6].

Over the past 15 to 20 years, advances in pharmacological treatment for IA have resulted in a marked improvement in patients' quality of life. The therapeutic feature of anti-inflammatory action [7] groups together a wide variety of chemically unrelated substances into a category known as nonsteroidal anti-inflammatory medications (NSAIDs). Sales of nonsteroidal anti-inflammatory medicines (NSAIDs) are around $6–$7 billion annually, making them the most profitable class of painkillers.

Fenoprofen is an anti-inflammatory drug used to treat conditions like gout, osteoarthritis, rheumatoid arthritis, and alkylosing spondylitis [8]. It works as well as other nonsteroidal anti-inflammatory medicines, if not better. It appears to be more nephrotoxic than other nonsteroidal anti-inflammatory medications [9], despite having similar efficacy. In the medical field, calcium salt is employed for the treatment of mild to moderate pain, as well as the alleviation of inflammatory conditions like arthritis. Platelet aggregation can be temporarily slowed by fenoprofen. Renal toxicity and a considerable gap between the dose needed for analgesia and that required for anti-inflammatory effect are two of fenoprofen's drawbacks when compared to other nonsteroidal anti-inflammatory drugs [10,11]. It is also used preventatively for vascular headaches, and can be used to alleviate dysmenorrhea and pain from nonrheumatic inflammatory diseases. Fenoprofen's anti-inflammatory activity is defined, and its significance in alleviating arthritis is discussed at length in this review. [12].

Pathophysiology of Inflammatory arthritis

Different types of inflammatory arthritis can be identified based on where the disease is thought to have originated or be most concentrated. While immune-mediated RA is characterized by preferential synovial hyperplasia in progressive joint destruction [13], osteoarthritis (OA) primarily displays hallmarks of a degenerative cartilage lesion. Fibrous connective and synovial tissues surround a joint made up of two or more bones that are linked with articular cartilage to decrease friction. The joint tissues are injured at multiple sites by these illnesses, leading to progressive cartilage deterioration, synovial inflammation, and subchondral osteosclerosis, according to recent research [14]. Therefore, it is crucial to investigate the process behind pathological abnormalities in particular compartments linked to the development of OA and RA. Abnormal production of degradable enzymes, cellular redox imbalance, and changes in microenvironment pH have all been linked to articular cartilage degeneration,

synovitis, and subchondral bone remodeling in injured joints (Fig. 1). New information about how to treat inflammatory arthritis can be gleaned from these pathological alterations. [15].

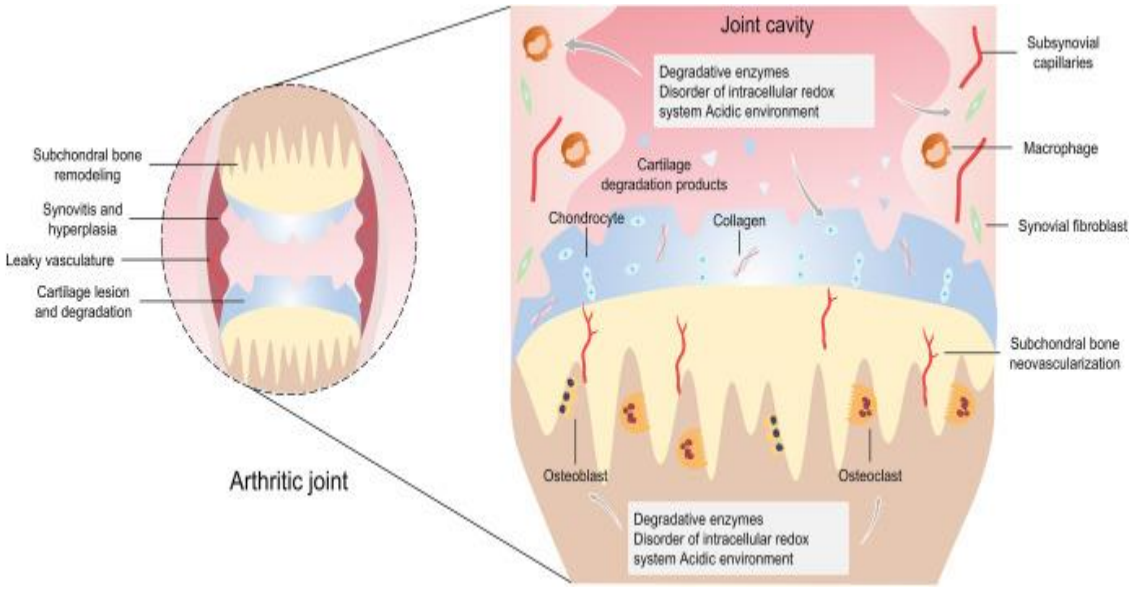

Fig. 1. Inflammatory arthritis causes changes in joint histopathology and associated cellular and molecular processes at several joint locations. Articular cartilage damage, synovial inflammation and hyperplasia, subchondral bone remodeling; cellular and molecular level abnormal activity and content of degrading enzymes; intracellular redox system imbalance; extracellular microenvironment acidification are all pathological changes in arthritic tissues.

IL-27 attenuates IL-23 mediated inflammatory arthritis

In the context of autoimmunity, interleukin 27 can promote or inhibit inflammation. Inhibition of Th17 differentiation is associated with IL-27's anti-inflammatory effects, while the impact of IL-27 on myeloid cells has received less attention. Here, we show that IL-27 suppresses IL-23-induced inflammation linked to Th17 cells and myeloid cell infiltration in joints and splenic myeloid populations of CD11b+ GR1+ and CD3CD11c+GR1 cells [17]. Myeloid cell counts in the spleen and bone marrow were found to be lower in individuals with an IL-27 anti-inflammatory response [18].

Inflammatory arthritis is just one of numerous rheumatic disorders linked to the proinflammatory cytokine IL-23. Conventional CD4+Th17 and non-conventional T cells that contribute to inflammation are both significantly influenced by IL-23 throughout their development and maturation [19,20]. Furthermore, IL-23 has direct effects on innate immune cells, causing synovial inflammation in mouse models of arthritis by increasing myeloid populations in the bone marrow [21]. Co-stimulatory pathways involving DAP12 and the immunoreceptor CLEC5A/MDL-1 are directly involved in IL-23's regulation of osteoclast progenitor growth [22,23]. Together, IL-23's induction of inflammation through IL-17A and the direct expansion of osteoclast progenitors contribute to the enhanced osteoclastogenesis and bone degradation that is observed [22,24]. The IL-23/IL-17A axis in inflammation is well-

known because it induces T cells that generate IL-17A and has various functions in autoimmunity [25]. Myeloid cell activation by IL-23, on the other hand, has received little attention.

Pathway of bone, cartilage and synovium destruction during RA

The immune complexes in the bloodstream are the site of the first step in the development of rheumatoid arthritis. Autoantigen and autoantibodies are introduced to the articular joints simultaneously during the transition period. [26]. Sentinel cells' innate immune response is triggered when they encounter a combination of autoantigen and IgG antibodies linked to Fc Receptor gamma (FcRg). Dendritic cells are typically the first line of defense to be activated. [27].

Autoantigen-bound dendritic cells then activate naive T cells, leading to the development of both T helper cells and regulatory T cells. Naive T cell cytokine production is stimulated by the co-stimulatory surface molecules CD80/86 and MHC II. [28]. Autoantibodies such as RF and ACPA are produced by B cells during differentiation of T helper cells and then travel through plasma cells and three distinct pathways to cause damage to bone, cartilage, and synovium. [29].

3.1. Bone erosion and destruction

Resorbing osteoclasts and generating osteoblast cells are responsible for the continual physiological process known as bone remodeling. In RA, bone production is disrupted, which impedes the healing process. [30]. Osteoclast genesis is triggered when macrophages, a kind of antigen-presenting cell, are activated by CD4 T helper cells and secrete the inflammatory cytokines TNF-alpha, interleukin-1, and interleukin-6. Resorption of trabecular and cortical bone releases calcium and other mineral elements into the blood system, thereby maintaining mineral homeostasis. Osteoclasts are multinucleated cells that arise from cytoplasmic fusion of osteoclast precursor cells. [31]. After that, osteoblast cells step in to make up for the lost bone. TNF-a, IL-1, and IL-6 are cytokines that stimulate and mediate bone resorption. [32]. These cytokines stimulate the production of M-CSF and RANKL by synovial joint cells, which in turn activates RANKL on osteoblast cells, which binds with its concomitant receptor RANK on osteoclast precursor cells, causing the precursor cells to differentiate into mature osteoclasts [33]. The ratio of osteoprotegerin (OPG) expressed from osteoblasts is also responsible for monitoring and controlling the overall stabilization of mineral content. Osteoprotegerin is a ligand-complementary osteoclast inhibitory factor that works in tandem with RANKL. Inactivating RANKL prevents osteoclasts from completing their route. Constant osteoclast differentiation occurs when the ratio of osteoprotogerins to RANKL decreases fast in RA. Matrix-attached mature osteoclasts produce hydrochloric acid and the proteolytic enzyme cathepsin K, which break down the connective tissue’s proteins osteonectin and aggrecan, leading to chronic joint deterioration [34].

3.2. Cartilage degradation

Extracellular matrix and a handful of cells make up most of the articular cartilage. Type II collagen, proteoglycans, and aggrecans [35] make up the bulk of ECM. Matrix metalloproteinases (MMPs) or matrixins, an enzyme that degrades cartilage, are secreted by synovial fibroblast cells in response to proinflammatory cytokines such as tumor necrosis factor alpha (TNF alpha), interleukin-1 (IL-1), and interleukin-6 (IL-6). There are 24 different varieties of matrix metalloproteinases, which are endopeptidases that rely on calcium and zinc. In RA, this group of enzymes serves as a reliable biomarker for cartilage degeneration [36]. Synovial chondrocytes and fibroblasts secrete MMPs. The joint surface is home to particular cell types that play a vital role in the degradation of cartilage tissue. Tissue Inhibitors of Metalloproteinase (TIMPs) slow down and block the effects of MMPs. [37]. To keep things in check, the levels of MMPs and TIMPs involved in cartilage metabolism are kept in check [38]. Bone polishing, osteophyte, or bone spur creation, occurs at bouchard's and heberden's nodes when cartilage deterioration causes friction between adjacent bones.

3.3. Synovial inflammation

The articular cavity is lubricated by synovial fluid, which is produced by synovium, the synovial membrane that lines the articular space. The intima is the middle layer of the synovial membrane, and it is lined by two types of synoviocytes: type A and type B intimal cells. [39]. Macrophages (Type A cells) are responsible for clearing out the synovial cavity, while synoviocytes (Type B cells) secrete synovial fluid components like hyaluronic acid and lubicin to keep things moving smoothly. [40]. Subsequent to the synoviocytes, you can find mast cells and capillary endothelial blood vessels. The subintima is a layer of fibroblasts and macrophages that provides structural support for the synovium. The synovium is the first-place inflammation occurs in rheumatoid arthritis. [41]. Cytokines secreted by synovial fibroblasts and macrophages play a significant role in synovial inflammation, the activation of synovial mononuclear cells, the development of new blood vessels (angiogenesis), and the onset of synovitis. Granular tissues (osteoclasts) populate the synovial membrane region known as the pannus [42]. Joint mice are tiny bits of cartilage or bone that break off and wander throughout the synovial cavity. Inflammation of the synovial membrane is exacerbated by this component. Fig. 2 shows the distinct chain of events that leads to the deterioration of bone, cartilage, and synovium due to RA.

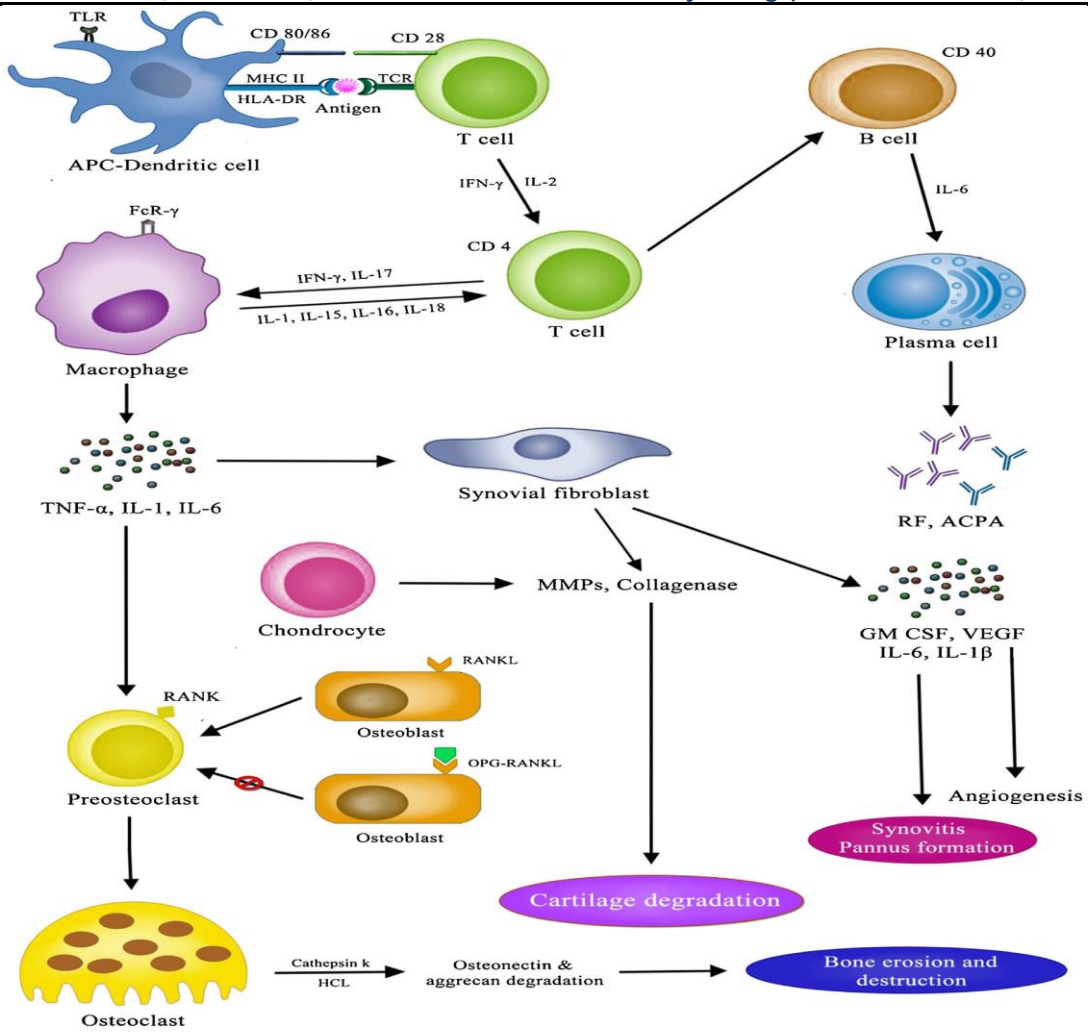

Fig. 2. The effect of damage to bone, cartilage, and synovium on the development of rheumatoid arthritis. Antigen presenting cell (APC) IL—interleukin, Interferon-gamma (IFN-g), Tumor necrosis factor a, often known as TNF-a, GM Granulocyte-macrophage colony-stimulating factor (CSF) and vascular endothelial growth factor (VEGF) The abbreviations for RANK and RANKL, respectively, stand for the receptor activator of nuclear factor kappa-B and the ligand for this protein, respectively. OPG—osteoprotegerin, Toll-like receptor (TLR) — toll-like receptor, Fc receptor gamma (FcR-g), Matrix metalloproteinases, or MMPs, Major histocompatibility complex (or MHC for short). Abbreviation for human leukocyte antigen; HLA "CD" stands for "cluster of differentiation," Rheumatoid factor and anti-cyclic citrullinated peptide antibody are abbreviations.

Fenoprofen Calcium

The FDA has approved the COX inhibitor fenoprofen calcium for the treatment of rheumatoid arthritis. Fenoprofen is commonly used in clinical settings to manage rheumatoid arthritis (RA), ankylosing spondylitis (AS), gout, and degenerative joint disease. Fenoprofen is well linked to plasma proteins and has a serum half-life of around 150-180 minutes. Fenoprofen glucuronide and 4-hydroxy-fenoprofen glucuronide are the main metabolites detected after oral treatment. [43]. Fenoprofen's precise mechanism of action is unknown, however it's thought to include blocking prostaglandin synthase. Fenoprofen has been shown to inhibit prostaglandin synthetase [44] when the enzyme is isolated from bovine seminal vesicles.

Fenoprofen calcium may be made in large quantities by the scalable synthesis route shown in Scheme 1. [45]. In order to obtain ketone FENO-003, 1-(3-hydroxyphenyl) ethan-1-one (FENO-001) is bromosubstituted with bromobenzene (FENO-002). The alcohol FENO-004 is created by reducing the ketone with NaBH4. Next, thionyl chloride is used to chlorinate the alcohol, creating the intermediate FENO-005, which is then converted into the nitrile FENO-006 via nucleophilic substitution with NaCN. To obtain Fenoprofen Calcium, the nitrile group of FENO-007 is hydrolyzed by a base, then the compound is treated with calcium carbonate in the presence of water.

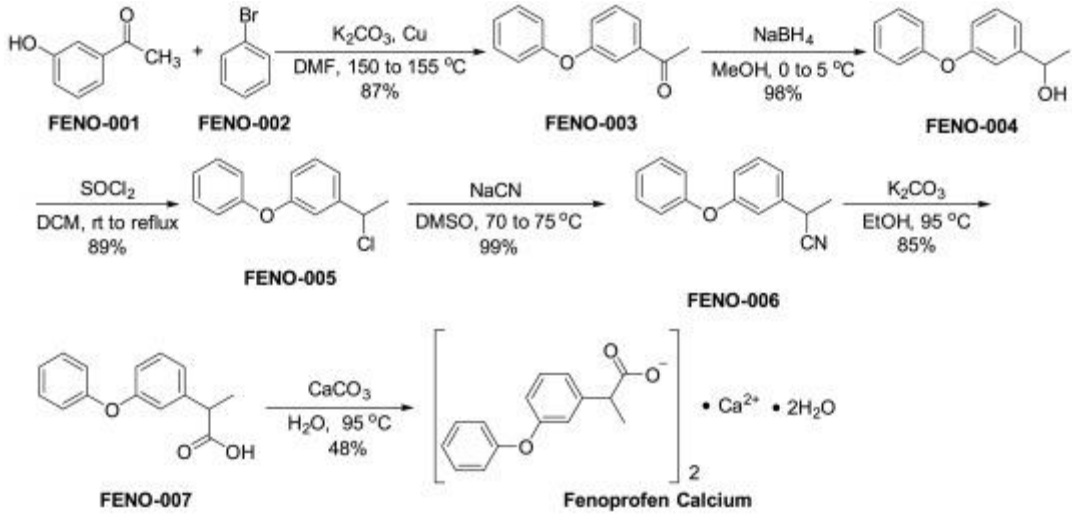

Fig. 3. Synthesis scheme of fenoprofen

Pharmacokinetics

When taken orally, fenoprofen is quickly absorbed. However, its absorption and bioavailability are reduced when given with food or milk. After being taken orally, peak plasma concentrations are reached in just a couple of hours. [46]. After being taken orally, the pain relief begins to kick in within 15-30 minutes and continues for four to six hours. Sweetman, 2003.[47] The fenoprofen calcium derivative is more widely utilized since it is easily absorbed, with a peak plasma level of 20–30 g/mL 2 hours after a single oral dose and a plasma half-life of 2–3 hours.112 The recommended daily intake is 2.4 g, and the medication is capsuled at 300 mg. Within the first 24 hours of treatment, steady-state plasma levels are achieved. Although fenoprofen is generally well-tolerated and has a low risk of causing occult gastrointestinal bleeding, its most common side effect is still dyspepsia. Most of the medication is eliminated in the urine as a glucuronide. [48].

Therapeutics of fenoprofen

Fenoprofen's anti-inflammatory effects in rheumatoid arthritis patients have been demonstrated by reports of decreased pain, increased grip strength, and decreased joint swelling, morning stiffness, and disease activity (as measured by both the investigator and the patient). Reductions in tenderness in response to pressure, as well as night pain, stiffness, swelling, and disease activity (as assessed by the patient and the investigator) in patients with osteoarthritis, demonstrate the anti-inflammatory and analgesic effects of fenoprofen. Pain reduction during

movement and during rest, as well as an increase in joint mobility, are additional indicators of these positive outcomes. Clinical studies have shown that fenoprofen is as effective as aspirin in reducing the aforementioned measures of disease activity in patients with rheumatoid arthritis and osteoarthritis, with the added benefit of causing fewer cases of mild gastrointestinal reactions (nausea, dyspepsia), and tinnitus. Whether fenoprofen or aspirin is safer for peptic ulcers is unknown. Fenoprofen's analgesic action has been shown to reduce pain intensity, boost pain relief, improve total analgesia scores, and have a lasting impact on patients with pain.

Fenoprofen-drug delivery for inflammatory arthritis treatment

Anti-inflammatory or analgesic drugs (given orally, topically, or intra-articularly), surgery, and physical therapy are the current pharmaceutical therapies for arthritis [49]. Poor water solubility, low cell permeability, unfavorable pharmacokinetics, random distribution in vivo, and unregulated drug degradation prior to reaching the target sites [50] are just some of the issues with the properties of these existing medications that contribute to the severely reduced bioavailability and low efficacy of anti-arthritic agents. Small sized nanoparticles with large specific surface areas and great loading efficiency have recently been the focus of research into fenoprofen-drug delivery. Nano-carriers may meet the demands for enhanced efficacy and fewer side effects if they possessed stimuli-responsive and targetable features in addition to their biocompatibility [50]. Drug delivery methods based on nanoparticles that respond to stimuli could prevent the onset of inflammatory arthritis by neutralizing the irritating factors present in dysfunctional tissues. [51,52]. Therefore, endogenous (enzyme, redox system, pH, etc.) stimuli are discussed below in relation to the advanced usage of responsive nanomaterials in the management of inflammatory arthritis (Fig. 2).

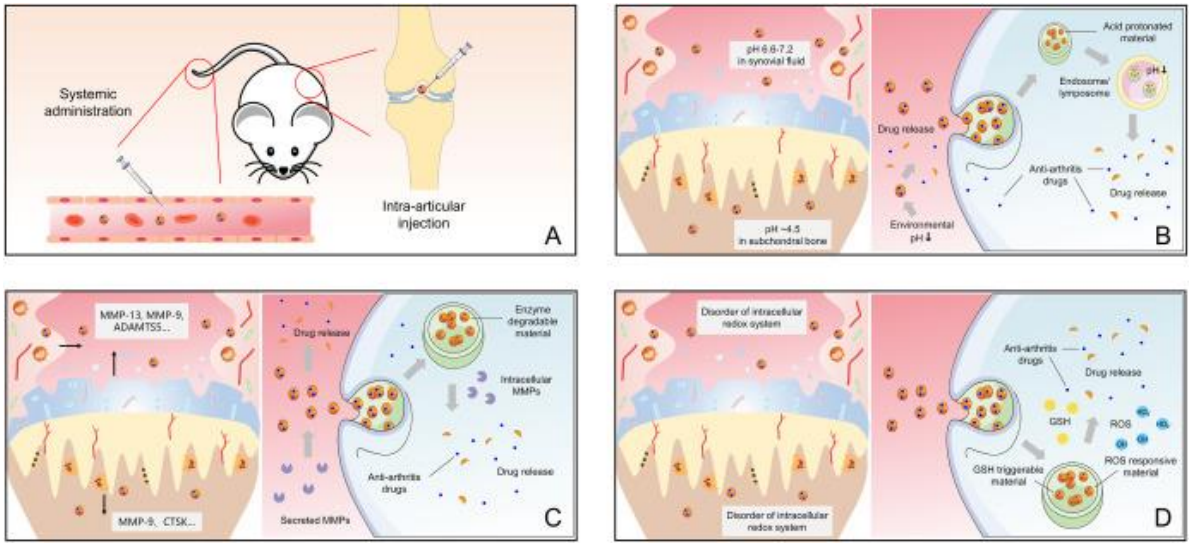

Fig. 4. The theory behind how medications that respond to internal stimuli can be produced. Systemic dosing and intra-articular injection are two examples of (A) routes of drug administration. (B) Drug release from pH-responsive materials extracellularly in acidic synovial fluid or acidic subchondral bone microenvironment; drug release from pH-responsive materials intracellularly in endosomes and lysosomes. (C) The cleavage of extracellular and extracellular aberrant enzymes from enzyme-responsive materials to trigger drug release. Drug release from redox-sensitive materials (D), brought on by aberrant signals due to a redox imbalance within the cell.

5. Treatment strategies

Drugs and non-drug treatments work together to alleviate the symptoms of inflammatory arthritis. [53,54]. Arthroplasty and other synthetic chemical treatments are common therapeutic options with good success rates. Formulated extracts of natural substances, such as phytocompounds, are also taken by vast populations for their therapeutic effects. Yoga, acupuncture, massage, and physiotherapy, among others, have been practiced in addition to these methods. [55].

5.1. Pharmacologic or medication-based therapy

Medication-based pharmacotherapy addresses the condition by alleviating symptoms including pain and edema and by halting its progression. [56]. Disease-modifying anti-rheumatic drugs (DMARDs), nonsteroidal anti-inflammatory drugs (NSAIDs), and corticosteroids are examples of pharmacologic agent classes. [57,58]. To further reduce RA mediators and inflammation, all of these medicines were taken singly or in combination. [59,60]. Side effects, reactive mechanisms, and NSAIDs, DMARDs, and corticosteroids are listed in Table 2.

5.1.1.1. NSAIDs

NSAIDs work by inhibiting the cyclooxygenase (COX) enzyme, which causes inflammation and pain. Both COX 1 and COX 2 are found in nature and serve as prostaglandin synthase enzymes. [61,62] Arachidonic acid's metabolites, prostaglandins (PGE2), play a pivotal role in rheumatoid arthritis (RA), particularly in the pathogenesis of synovial inflammation and the degeneration of articular cartilage.[63]. As a result, NSAIDs inhibit COX 2, which reduces inflammation. These medications are used as a first line of defense in the absence of RA risk factors such as rheumatoid factor (RF), anti-cyclic phosphorylcholine antigen (ACPA), bone erosion, mobility loss, multiple swollen joints, and a common DR4 epitope. For faster healing, it could be used with a little number of glucocorticoids.[64].

5.1.1.2. DMARDs

Conventional synthetic DMARDs and biological DMARDs are the two main types of disease-modifying anti-rheumatic medicines. The medication classes all respond to RA in their own special ways. Biological DMARDs mimic the effects of immune system-generated chemicals. Common examples of biological DMARDs that mimic the action of TNF- inhibitors include adalimumab and infliximab [65]. Typically, it attacks antigen-presenting cell (APC) and B-cell-surface CD molecules and soluble cytokines. Traditional DMARDs, on the other hand, typically function within the cell itself [66]. In RA, methotrexate is the drug of choice for conventional first treatment. Nonetheless, forty percent of RA sufferers show no response to the treatment [67].

5.1.1.3. Corticosteroids

The tiny, hydrophobic chemicals known as corticosteroids have anti-inflammatory and immunoregulatory effects. Prostaglandins, leukotrienes, and other inflammatory chemicals are suppressed. [68]. However, it requires daily use to alleviate symptoms. When nonsteroidal anti-inflammatory drugs (NSAIDs) and disease-modifying antirheumatic drugs (DMARDs) fail to control RA symptoms, this is an adjunctive treatment option. The adrenal corticosteroid hormone cortisol has a synthetic analogue. Stress and inflammation are linked to inadequate glucocorticoid release by the adrenal gland. Here, glucocorticoids are thought to play a pivotal role in the development of RA [69].

5.1.2. Phytocompounds

In order to get a long-term cure, we need to step up the pharmacotherapies by including natural items like herbs. Numerous plant species have been identified as possessing active anti-arthritic chemicals, and certain formulations have been used as substitutes for commercial medications. Synthetic therapeutic approaches either inhibit tissue degrading enzymes or modify a specific cell or inflammatory mediator. [70]. However, restoring a functional immune system has been difficult so far. The use of natural phytocompounds may be able to overcome this disadvantage. There are several benefits of using plant-based remedies rather than conventional medical interventions like drugs and surgery. Disease-fighting phytochemicals have multiple uses and are quite safe to use. [71,72].

5.3. Surgery

Joints of the hands and foot, including the proximal interphalangeal (PIP) and metacarpophalangeal (MCP) joints, are frequently affected by rheumatoid arthritis. When dealing with severe disease, such as complete joint degeneration, arthroscopy can provide instantaneous pain relief. [73,74]. When medical therapy fails to alleviate RA symptoms, surgery to remove diseased tissue, fuse joints, or replace affected joints (such as the proximal interphalangeal, hip, tendon, or knee) has been the standard practice for many years. Arthroscopic procedures such as joint resurfacing, osteotomy, synovectomy, and arthrodesis were used to treat RA at varying stages. Joint resurfacing, also known as partial or localized joint replacement surgery, is a subset of arthroscopy in which only the damaged or diseased sections of a joint are replaced rather than the entire joint. [75]. Some severe cases, such as the degeneration of the foot's metatarsophalangeal joints due to rheumatoid arthritis, may not be effectively treated with joint resurfacing or other surgical techniques. A weil metatarsal osteotomy, in which the patient's weight is transferred away from the injured joint, is an effective surgical treatment for such problems [76]. Another surgical option for treating diseases mediated by the synovium is called a synovectomy. Synovial membrane disease is treated by removing some or all of it from the affected joint. However, it is not sufficient for improving the flexibility [77]. Arthrodesis, also known as joint fusion surgery, is typically performed for an arthritic ankle joint by fusing the ends of the joint together. When osteoarthritis or rheumatoid arthritis have progressed to this later stage, this is one of the most effective operations available. The joint's complex anatomy, however, presents challenges during surgical procedures [78]. As an inflammatory illness that affects joints symmetrically throughout the body, RA

patients would not benefit as much from arthroscopy or the excision of bone spurs as osteoarthritis patients would [79].

5.2. Gene therapy

Over the past decade, there have been substantial developments in the treatment of rheumatoid arthritis. Despite widespread use, treatments like TNF inhibitors and various anti-inflammatory drugs have drawbacks include harmful effects, protracted therapy, frequent prescription, and no long-term curative impact. Targeted gene therapy, which is more specific and optimal, has been successfully studied in animal models to circumvent these challenges [80]. Since multiple genes contribute to RA, targeting one gene with gene therapy won't help. Here, DNA fragments encoding anti-inflammatory or other arthritis suppressor compounds, such as IL-35, an immunosuppressive cytokine, are electro transferred into the body to express their function in the body by producing immunosuppressive agents against hyperactive immune systems. In terms of both expression and distribution of the chemical, gene therapy has significant benefits over direct administration [80]. The MHC II locus most crucial to RA susceptibility is the human leukocyte antigen (HLA)-DR locus. Other coding, non-coding, and promoter genes targeted in rheumatoid arthritis gene therapy include PTPN22, PAD14, TGF-, FcR--III, STAT4, TRAF1-C5, and TNF, IL-6 [81].

5.4. Complementary and alternative therapies

For the sake of prevention and safety, some non-pharmacological alternatives of RA therapy have been tried and tested. Disease management can be improved by adopting a healthy lifestyle, including regular exercise, a balanced diet, and positive mental attitudes. To lessen muscular reactivity, boost the metabolism, and enhance muscle and joint functioning, massage treatment involves applying pressure and making slighter motions to the deeper layer of muscles and bone joints. Patients with rheumatoid arthritis benefit from massage therapy with sesame oil because of its anti-inflammatory properties. Yog asanas are a sequence of postures practiced in order to bring the body's systems into balance. To prevent the spread of RA, practitioners strike such as Pawanmuktasana, Shavasana, and Pranayama [82]. Telles et al. [83] report that rheumatoid factors are reduced in yoga practitioners. The Chinese martial art of tai chi emphasizes slow, deliberate motion and deep breathing. It helps us build muscle, strengthen our lower body, and increase flexibility in our ankles, hips, and knees [84]. In acupuncture, tiny needles are used to activate acupuncture sites on the skin. Bee venom and acupuncture needles, two active substances, were utilized successfully to treat rheumatoid arthritis [85]. Alternative or complementary treatments have a low risk of harmful side effects. These treatments may complement conventional RA care, but they are not intended to serve as a substitute for it.

Discussion

Another prevalent form of arthritis is rheumatoid arthritis. Rheumatoid arthritis affects fewer than 2% of the global population, however there is still no known permanent cure or recovery. Focused treatment has a better chance of success if the condition is diagnosed early. We have developed new targeted therapies due to our comprehension of the pathophysiology of RA, namely the function of cytokine interaction in anatomical change. Myelopoiesis in the spleen, myeloid cell infiltration, and joint inflammation induced by interleukin (IL) were all greatly attenuated by overexpression of interleukin (IL). Rheumatoid arthritis patients undergoing arthroscopies to have their joints surgically altered or amputated. It is a true systemic sickness affecting several body systems. An integrated approach of pharmacological and non-pharmacological therapy may give beneficial outcomes, and the exceptional success of TNF specific DMARDs in pharmacological therapy for RA is cause for optimism. However, there is still a need for the development of novel modalities and helpful techniques to alleviate the contrasting side effects.

Conclusion and prospect

In conclusion, COX, JAK, GR, etc., are the primary therapeutic targets for rheumatoid arthritis. The therapeutic medicines and clinical efficacy of RA have gradually improved with the emergence of small molecule targeted medications. By negatively limiting the growth of myeloid cell subsets, IL-27 plays a vital role in managing IL-23 driven joint inflammation and its immunosuppressive effects on IL-23-dependent myelopoiesis in the bone marrow and its progression to inflammatory arthritis.

While nonsteroidal anti-inflammatory medicines (NSAIDs) and analgesics can provide rapid symptom relief for patients with RA who are already experiencing joint swelling and discomfort, they cannot stop further bone deterioration. As soon as a diagnosis of RA is made, the patient should begin using a disease-modifying medicine such methotrexate. Glucocorticoid has both positive and negative effects. Bone loss can be slowed with proper use, but there are several potential negative outcomes to consider. Low-dose glucocorticoids, such as betamethasone, can be given for a limited duration for patients who are making poor recovery and have an apparent inflammatory response. The development of potent, but pricey, biologics has been a major breakthrough in the treatment of rheumatoid arthritis. This review's discussion of the synthesis and clinical application of small molecule medications approved to treat RA may spark new drug and strategy development for the treatment of RA.

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